# Clinical trial results:
# A randomized, double blind, placebo controlled, parallel group, multiple dose, induction study to evaluate the safety, tolerability and optimal dose of ABX464 compared with placebo in patients with moderate to severe ulcerative colitis who have inadequate response, loss of response, or intolerance with at least one of the following agents: immunosuppressant treatment (i.e. azathioprine, 6-mercaptopurine, methotrexate), tumor necrosis factor alpha [TNF-] inhibitors, vedolizumab, JAK inhibitors and/or corticosteroid treatment.

## Summary

| | |
|---|---|
| EudraCT number | 2018-003558-26 |
| Trial protocol | FR SI CZ DE SK HU PL BE GB IT |
| Global end of trial date | 31 August 2022 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 20 February 2023 |
| First version publication date | 20 February 2023 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ABX464-103 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03760003 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | ABIVAX |
| Sponsor organisation address | 7-11 Boulevard Haussmann, Paris, France, 75009 |
| Public contact | Clinical Operations, Abivax, +33 15383 0961, Paul.Gineste@abivax.com |
| Scientific contact | Clinical Operations, Abivax, +33 15383 0961, Paul.Gineste@abivax.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 | 31 August 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 April 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 August 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to determine an optimal ABX464 dose to be used in moderate to severe active ulcerative colitis patients who have failed or are intolerant to immunomodulators, Anti-TNFα, vedolizumab, JAK inhibitors and/or corticosteroids by comparing the mean change from baseline in the MMS at week 8 between each ABX464 group and placebo.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form (ICF)

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 31 May 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 52 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 70 |
| Country: Number of subjects enrolled | Slovakia: 18 |
| Country: Number of subjects enrolled | Slovenia: 3 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | Austria: 6 |
| Country: Number of subjects enrolled | Belgium: 8 |
| Country: Number of subjects enrolled | Czechia: 14 |
| Country: Number of subjects enrolled | France: 31 |
| Country: Number of subjects enrolled | Germany: 16 |
| Country: Number of subjects enrolled | Hungary: 22 |
| Country: Number of subjects enrolled | Italy: 21 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | Serbia: 5 |
| Country: Number of subjects enrolled | Ukraine: 32 |
| Country: Number of subjects enrolled | United States: 2 |

| | |
|---|---|
| Worldwide total number of subjects | 254 |
| EEA total number of subjects | 210 |

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) | 239 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A  total of 355 patients were enrolled in the study. Of these, 101 patients were screen failures and 1 patient was a Baseline failure (the patient signed informed consent but withdrew before the baseline visit).

### Period 1

| | |
|---|---|
| Period 1 title | Randomized 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 |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

2 capsules of 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:

once daily during a meal with a glass of water

| | |
|---|---|
| **Arm title** | 25mg ABX464 |

Arm description:

1 capsule of 25mg ABX464 + 1 capsule of Placebo

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | obefazimod |
| Investigational medicinal product code | ABX464 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water.

| | |
|---|---|
| **Arm title** | 50mg ABX464 |

Arm description:

1 capsule of 50mg ABX464 + 1 capsule of Placebo

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | obefazimod |
| Investigational medicinal product code | ABX464 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water

| | |
|---|---|
| **Arm title** | 100mg ABX464 |

Arm description:

2 capsules of 50mg ABX464

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | obefazimod |
| Investigational medicinal product code | ABX464 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water.

| **Number of subjects in period 1** | Placebo | 25mg ABX464 | 50mg ABX464 |
|---|---|---|---|
| Started | 64 | 63 | 63 |
| FAS | 64 | 61 | 63 |
| Completed | 57 | 58 | 53 |
| Not completed | 7 | 5 | 10 |
| Consent withdrawn by subject | 2 | - | 3 |
| Physician decision | - | 1 | - |
| Adverse event, non-fatal | 4 | 1 | 6 |
| Pregnancy | - | 2 | - |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | 1 | - | - |
| Protocol deviation | - | 1 | - |

| **Number of subjects in period 1** | 100mg ABX464 |
|---|---|
| Started | 64 |
| FAS | 64 |
| Completed | 54 |
| Not completed | 10 |
| Consent withdrawn by subject | 5 |

| | |
|---|---|
| Physician decision | - |
| Adverse event, non-fatal | 5 |
| Pregnancy | - |
| Lost to follow-up | - |
| Lack of efficacy | - |
| Protocol deviation | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| 2 capsules of Placebo | |
| Reporting group title | 25mg ABX464 |
| Reporting group description: | |
| 1 capsule of 25mg ABX464 + 1 capsule of Placebo | |
| Reporting group title | 50mg ABX464 |
| Reporting group description: | |
| 1 capsule of 50mg ABX464 + 1 capsule of Placebo | |
| Reporting group title | 100mg ABX464 |
| Reporting group description: | |
| 2 capsules of 50mg ABX464 | |

| Reporting group values | Placebo | 25mg ABX464 | 50mg ABX464 |
|---|---|---|---|
| Number of subjects | 64 | 63 | 63 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 60 | 58 | 60 |
| From 65-84 years | 4 | 5 | 3 |
| Age continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 41.1 | 41.5 | 40.2 |
| standard deviation | ± 14.43 | ± 14.16 | ± 13.94 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 24 | 22 | 36 |
| Male | 40 | 41 | 27 |

| Reporting group values | 100mg ABX464 | Total | |
|---|---|---|---|
| Number of subjects | 64 | 254 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 61 | 239 | |
| From 65-84 years | 3 | 15 | |
| Age continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 42.2 | | |
| standard deviation | ± 12.34 | - | |

| | | | |
|---|---|---|---|
| Gender categorical<br>Units: Subjects | | | |
| Female | 23 | 105 | |
| Male | 41 | 149 | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Full analysis set [FAS] |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The FAS contained all patients included in the study who had received at least 1 dose of the study treatment, and who had Baseline data for at least 1 efficacy variable.

| **Reporting group values** | Full analysis set [FAS] | | |
|---|---|---|---|
| Number of subjects | 252 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 237 | | |
| From 65-84 years | 15 | | |
| Age continuous | | | |
| Age (years) | | | |
| Units: years | | | |
| arithmetic mean | 41.2 | | |
| standard deviation | ± 13.67 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 104 | | |
| Male | 148 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| 2 capsules of Placebo | |
| Reporting group title | 25mg ABX464 |
| Reporting group description: | |
| 1 capsule of 25mg ABX464 + 1 capsule of Placebo | |
| Reporting group title | 50mg ABX464 |
| Reporting group description: | |
| 1 capsule of 50mg ABX464 + 1 capsule of Placebo | |
| Reporting group title | 100mg ABX464 |
| Reporting group description: | |
| 2 capsules of 50mg ABX464 | |
| Subject analysis set title | Full analysis set [FAS] |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The FAS contained all patients included in the study who had received at least 1 dose of the study treatment, and who had Baseline data for at least 1 efficacy variable. | |

### Primary: Reduction from Baseline in MMS at Week 8.

| | |
|---|---|
| End point title | Reduction from Baseline in MMS at Week 8. |
| End point description: | |
| Change from baseline to week 8 | |
| End point type | Primary |
| End point timeframe: | |
| Week 8 | |

| End point values | Placebo | 25mg ABX464 | 50mg ABX464 | 100mg ABX464 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 59 | 54 | 58 |
| Units: Least squares mean | | | | |
| least squares mean (confidence interval 95%) | -1.9 (-2.4 to -1.5) | -3.1 (-3.6 to -2.6) | -3.2 (-3.7 to -2.7) | -2.9 (-3.4 to -2.5) |

## Statistical analyses

| Statistical analysis title | ANCOVA MODEL PLACEBO vs ABX464 25 mg |
|---|---|
| Comparison groups | Placebo v 25mg ABX464 |
| Number of subjects included in analysis | 119 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANCOVA |

| Statistical analysis title | ANCOVA MODEL PLACEBO vs ABX464 50 mg |
|---|---|
| Comparison groups | Placebo v 50mg ABX464 |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANCOVA |

| Statistical analysis title | ANCOVA MODEL PLACEBO vs ABX464 100 mg |
|---|---|
| Comparison groups | 100mg ABX464 v Placebo |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | ANCOVA |

| Secondary: CLINICAL RESPONSE | |
|---|---|
| End point title | CLINICAL RESPONSE |
| End point description:<br>Number of patients with clinical response at week 8 | |
| End point type | Secondary |
| End point timeframe:<br>Week 8 | |

| End point values | Placebo | 25mg ABX464 | 50mg ABX464 | 100mg ABX464 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 64 | 61 | 63 | 64 |
| Units: Number | | | | |
| clinical reponse | 22 | 38 | 37 | 32 |

| End point values | Full analysis set [FAS] | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 252 | | | |
| Units: Number | | | | |
| clinical reponse | 129 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: CLINICAL REMISSION

| End point title | CLINICAL REMISSION |
|---|---|
| End point description:<br>Number of patients in clinical remission at week 8 | |
| End point type | Secondary |
| End point timeframe:<br>Week 8 | |

| End point values | Placebo | 25mg ABX464 | 50mg ABX464 | 100mg ABX464 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 64 | 61 | 63 | 64 |
| Units: Number of patients | | | | |
| Clinical remission | 8 | 16 | 11 | 16 |

| End point values | Full analysis set [FAS] | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 252 | | | |
| Units: Number of patients | | | | |
| Clinical remission | 51 | | | |

## Statistical analyses

| Statistical analysis title | Mantel-Haenszel Chi Square Test |
|---|---|
| Comparison groups | 100mg ABX464 v 50mg ABX464 v 25mg ABX464 v Placebo v Full analysis set [FAS] |

| | |
|---|---|
| Number of subjects included in analysis | 504 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | ≥ 0.5 |
| Method | Mantel-Haenszel |

## Secondary: ENDOSCOPIC IMPROVEMENT

| | |
|---|---|
| End point title | ENDOSCOPIC IMPROVEMENT |
| End point description: Number of patients with endoscopic improvement | |
| End point type | Secondary |
| End point timeframe: Week 8 | |

| End point values | Placebo | 25mg ABX464 | 50mg ABX464 | 100mg ABX464 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 64 | 61 | 63 | 64 |
| Units: Number of patients | | | | |
| Endoscopic Improvement | 8 | 20 | 21 | 24 |

| End point values | Full analysis set [FAS] | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 252 | | | |
| Units: Number of patients | | | | |
| Endoscopic Improvement | 73 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: ENDOSCOPIC REMISSION

| | |
|---|---|
| End point title | ENDOSCOPIC REMISSION |
| End point description: Number of patients with endoscopic remission | |
| End point type | Secondary |
| End point timeframe: Week 8 | |

| End point values | Placebo | 25mg ABX464 | 50mg ABX464 | 100mg ABX464 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 64 | 61 | 63 | 64 |
| Units: Number of patients | | | | |
| Endoscopic Remission | 5 | 4 | 5 | 2 |

| End point values | Full analysis set [FAS] | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 252 | | | |
| Units: Number of patients | | | | |
| Endoscopic Remission | 16 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

OVERALL

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Safety Analysis Set (SAF): Placebo treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

| | |
|---|---|
| Reporting group title | 100 mg |

Reporting group description:

Safety Analysis Set (SAF): 100 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

| | |
|---|---|
| Reporting group title | 50 mg |

Reporting group description:

Safety Analysis Set (SAF): 50 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

| | |
|---|---|
| Reporting group title | 25 mg |

Reporting group description:

Safety Analysis Set (SAF): 25 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

| Serious adverse events | Placebo | 100 mg | 50 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 4 / 64 (6.25%) | 4 / 63 (6.35%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (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 |
| Myocardial infarction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (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 | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | 25 mg | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Placebo | 100 mg | 50 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 64 (46.88%) | 45 / 64 (70.31%) | 38 / 63 (60.32%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|---|---|---|
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Surgical and medical procedures | | | |
| Tooth extraction | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 2 / 63 (3.17%) |
| occurrences (all) | 0 | 1 | 2 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 64 (3.13%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| Mite allergy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Breast cyst | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Investigations | | | |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 64 (1.56%) | 2 / 63 (3.17%) |
| occurrences (all) | 2 | 1 | 2 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 2 / 63 (3.17%) |
| occurrences (all) | 0 | 1 | 2 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 64 (3.13%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood fibrinogen increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood lactate dehydrogenase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematocrit decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Human chorionic gonadotropin increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intraocular pressure increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 2 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prostatic specific antigen increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Troponin T increased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Left ventricular hypertrophy | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 64 (7.81%) | 27 / 64 (42.19%) | 19 / 63 (30.16%) |
| occurrences (all) | 5 | 29 | 21 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 64 (3.13%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Syncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Parosmia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Peripheral sensorimotor neuropathy | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 2 | 1 | 1 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Eczema eyelids | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 9 / 64 (14.06%) | 4 / 63 (6.35%) |
| occurrences (all) | 4 | 9 | 5 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 4 / 64 (6.25%) | 3 / 63 (4.76%) |
| occurrences (all) | 0 | 4 | 4 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 1 / 64 (1.56%) | 4 / 63 (6.35%) |
| occurrences (all) | 4 | 1 | 4 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 5 / 64 (7.81%) | 2 / 63 (3.17%) |
| occurrences (all) | 1 | 5 | 2 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 64 (3.13%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 2 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 1 | 0 | 1 |
| Faeces discoloured | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Intestinal fistula | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Intestinal polyp | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis migration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Liver injury | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 2 / 64 (3.13%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 2 / 63 (3.17%) |
| occurrences (all) | 0 | 2 | 2 |
| Rash | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Erythema nodosum | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Pityriasis rosea | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| Chromaturia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal colic | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 5 / 64 (7.81%) | 1 / 63 (1.59%) |
| occurrences (all) | 3 | 6 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 5 / 64 (7.81%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 3 / 64 (4.69%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Coccydynia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Tendon disorder | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 3 / 63 (4.76%) |
| occurrences (all) | 0 | 1 | 3 |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 2 | 0 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatophytosis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes virus infection | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes zoster | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pyoderma | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 64 (1.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| | | | |
|---|---|---|---|
| Dehydration | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Fluid retention | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperlipasaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 0 / 64 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Iron deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 64 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| **Non-serious adverse events** | 25 mg | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 62 (53.23%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Surgical and medical procedures | | | |
| Tooth extraction | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Immune system disorders | | | |
| Mite allergy | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Breast cyst | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Glutamate dehydrogenase increased | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Neutrophil count increased | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| White blood cell count increased | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood cholesterol increased | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood fibrinogen decreased | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Blood fibrinogen increased | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Blood lactate dehydrogenase increased | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Haematocrit decreased | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Haemoglobin decreased | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Hepatic enzyme increased | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Human chorionic gonadotropin increased | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Intraocular pressure increased | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Prostatic specific antigen increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Troponin T increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Left ventricular hypertrophy | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---|---|---|
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 62 (20.97%) | | |
| occurrences (all) | 14 | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Parosmia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Peripheral sensorimotor neuropathy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| Eye disorders | | | |
| Eczema eyelids | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 4 | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Proctalgia | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 62 (3.23%) | | | |
| occurrences (all) | 2 | | | |
| Gastrooesophageal reflux disease | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Constipation | | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | | |
| occurrences (all) | 2 | | | |
| Dyspepsia | | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | | |
| occurrences (all) | 2 | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Abdominal distension | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Faeces discoloured | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Frequent bowel movements | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |
| Gastritis erosive | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Intestinal fistula | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Intestinal polyp | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Melaena | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Odynophagia | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis migration | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Liver injury | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all)<br><br>Erythema nodosum<br>subjects affected / exposed<br>occurrences (all)<br><br>Ingrowing nail<br>subjects affected / exposed<br>occurrences (all)<br><br>Night sweats<br>subjects affected / exposed<br>occurrences (all)<br><br>Pityriasis rosea<br>subjects affected / exposed<br>occurrences (all)<br><br>Skin mass<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0<br><br>0 / 62 (0.00%)<br>0<br><br>1 / 62 (1.61%)<br>1<br><br>0 / 62 (0.00%)<br>0<br><br>0 / 62 (0.00%)<br>0<br><br>0 / 62 (0.00%)<br>0 | | |
| Renal and urinary disorders<br>Chromaturia<br>subjects affected / exposed<br>occurrences (all)<br><br>Renal colic<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0<br><br>0 / 62 (0.00%)<br>0 | | |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1 | | |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain | 1 / 62 (1.61%)<br>1<br><br>0 / 62 (0.00%)<br>0 | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Coccydynia | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | | |
|---|---|---|---|---|
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Cystitis | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Dermatophytosis | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Escherichia urinary tract infection | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Herpes virus infection | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Paronychia | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Pyoderma | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Rhinitis | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Tonsillitis | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Tooth abscess | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences (all) | 1 | | | |

| | | | |
|---|---|---|---|
| Vulvovaginal mycotic infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Metabolism and nutrition disorders<br>Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 2 / 62 (3.23%)<br>2 | | |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1 | | |
| Folate deficiency<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1 | | |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Dehydration<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Fluid retention<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Hyperlipasaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| Iron deficiency<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 16 July 2019 | Clinical response defined as reduction in Mayo score of greater than or equal to 3 points was changed to at least 2 points (Sections 2.0 and 8.2.2).<br>For enrollment of patients in the study, moderately to severely active UC definition based on MMS range of 4 to 9 was modified to range 5 to 9 (Sections 2.0 and 9.3.1). |
| 07 November 2019 | Assessment of T3, T4 and TSH levels by local laboratory were added at Baseline, Day 57, Day 113 (Table 1). |
| 12 December 2019 | Addition of exclusion criterion: Patients who received live vaccine 30 days or fewer before first dose of study treatment and/or who is planning to receive such a vaccine during the study duration. |
| 11 January 2020 | US eligible patients were to be randomized only to once daily ABX464 50 mg, ABX464 25 mg, or placebo. US patients were not eligible to receive ABX464 100 mg once daily (Sections 9.1 and 9.4.3.1).<br>Patients were required to have the following additional laboratory parameters obtained within 14 days prior to Baseline: creatinine clearance ≥90 mL min-1 by the Cockcroft-Gault equation within 60 days prior to baseline, fibrinogen >0.9 × lower limit of normal and international normalized ratio ≤1.2 (if no anticoagulant therapy) (Section 9.3.1).<br>Prohibited concomitant medications were updated to include drugs that inhibit or induce CYP1A2 and drugs that inhibit UGTIA9 activity and inhibitors or substrates of OATP1B1/1B3 transporters (Section 9.4.5).<br>Patients enrolled in the US were not rolled over an open label extension study (ABX464-104). Patients were to be treated for 16 weeks and an end of study visit was to be performed within a week after last dosing (Section 9.1). |
| 01 June 2020 | The definition of clinical remission (a secondary endpoint) was changed (Sections 2.0 and 8.2.2).<br>Exclusion criterion added: patients who received live vaccine 30 days or fewer before first dose of study treatment and/or who is planning to receive such a vaccine during the study duration (Section 9.3.2).<br>Prohibited concomitant medications were updated to include drugs that inhibit or induce CYP1A2 and drugs that inhibit UGTIA9 activity and inhibitors of OATP1B1/1B3 transporters (Section 9.4.5). |
| 30 July 2020 | Similar to AMEND 2, (dated 01 june 2020) |
| 08 October 2020 | Similar to AMEND 2, (dated 01 june 2020) |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial?  No

## Limitations and caveats

None reported