# Clinical trial results:
# Randomised, double-blind, vehicle controlled trial comparing Amphotericin B 100.000 I.E./g oral gel vs. Ampho-Moronal® suspension vs. modified vehicle to suspension in adult patients with oropharyngeal candidiasis

## Summary

| | |
|---|---|
| EudraCT number | 2013-000371-32 |
| Trial protocol | DE |
| Global end of trial date | 11 April 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 May 2020 |
| First version publication date | 14 May 2020 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 13-02/AM-MG |

### Additional study identifiers

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

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Dermapharm AG |
| Sponsor organisation address | Lil-Dagover Ring 7, Gruenwald, Germany, 82031 |
| Public contact | Clinical Research Department, Dermapharm AG, Clinicaltrials.Dermapharm@dermapharm.com |
| Scientific contact | Clinical Research Department, Dermapharm AG, Clinicaltrials.Dermapharm@dermapharm.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 | 08 April 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 April 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 April 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the safety and efficacy of a new dosage form containing Amphotericin B on an oral gel base in comparison to the approved Ampho-Moronal® suspension. The study aimed to show therapeutic non-inferiority of the test preparation compared to the reference preparation and superiority of both active medications over the vehicle.

Protection of trial subjects:

The study was conducted in accordance with the principles of ICH GCP, the declaration of Helsinki, as well as all other applicable ethical and legal requirements. The reference product Ampho Moronal suspension is already registered for the application in the study indication and commercially available for years in Germany. For the purpose of approval the efficacy and safety of this medicinal product has already been shown in clinical trials. Any patient with lack of efficacy and/or deterioration of symptoms could stop treatment at any moment based on the clinical judgment of the investigator or on his/ her own request and without giving reasons. The planned procedures within the trial represented no special risks to the patients as, apart from usual medicinal practice procedures, no additional invasive procedures were planned.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 October 2014 |
| 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 | Germany: 391 |
| Worldwide total number of subjects | 391 |
| EEA total number of subjects | 391 |

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) | 214 |
| From 65 to 84 years | 172 |
| 85 years and over | 5 |

## Subject disposition

### Recruitment

Recruitment details:

Multi-centric study in Germany; first volunteer enrolled: 11-Nov-2014; date of last completion: 11-Apr-2019

### Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:
Men and women aged ≥ 18 years; clinical signs and symptoms of oropharyngeal candidiasis (OPC) with a sum score of ≥ 4 of
the parameters erythematous areas, removable white patches, soreness/burning and extent of oral lesions (single scores between 0 and 3); existence of predisposing risk factors for OPC

### Period 1

| | |
|---|---|
| Period 1 title | Treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

The preparations were filled in brown glass bottles and labelled indistinguishably. All study preparations were coloured and contained flavouring substances. So the investigator and patients could not draw any conclusion from colour and flavour about the preparation with which they were treated.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Test product |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Amphotericin B oral gel |
| Investigational medicinal product code | A07AA07 |
| Other name | |
| Pharmaceutical forms | Oromucosal gel |
| Routes of administration | Buccal use |

Dosage and administration details:

1 g four times a day into the oral cavity

| | |
|---|---|
| **Arm title** | Reference product |

Arm description: -

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Ampho-Moronal Suspension |
| Investigational medicinal product code | A07AA07 |
| Other name | |
| Pharmaceutical forms | Oromucosal suspension |
| Routes of administration | Buccal use |

Dosage and administration details:

1 ml four times a day into the oral cavity

| | |
|---|---|
| **Arm title** | Vehicle |

Arm description: -

| | |
|---|---|
| Arm type | Placebo |

| | |
|---|---|
| Investigational medicinal product name | Modified vehicle to reference product |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oromucosal suspension |
| Routes of administration | Buccal use |

Dosage and administration details:

1 g four times a day into the oral cavity

| **Number of subjects in period 1** | Test product | Reference product | Vehicle |
|---|---|---|---|
| Started | 126 | 133 | 132 |
| Completed | 113 | 118 | 114 |
| Not completed | 13 | 15 | 18 |
| Physician decision | 1 | 4 | 1 |
| Consent withdrawn by subject | 3 | 5 | 4 |
| Adverse event, non-fatal | 6 | 5 | 6 |
| Lost to follow-up | 1 | - | 4 |
| Healing | 1 | - | 1 |
| Lack of efficacy | 1 | 1 | 2 |

| **Period 2** | |
|---|---|
| Period 2 title | Follow up |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Subject, Data analyst |
| **Arms** | |
| Are arms mutually exclusive? | Yes |
| **Arm title** | Test - Follow up |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Reference Follow up |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Vehicle Follow up |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| **Number of subjects in period 2** | Test - Follow up | Reference Follow up | Vehicle Follow up |
|---|---|---|---|
| Started | 113 | 118 | 114 |
| Completed | 110 | 111 | 110 |
| Not completed | 3 | 7 | 4 |
| Consent withdrawn by subject | 3 | 7 | 4 |

## Baseline characteristics

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Test product |
| Reporting group description: - | |
| Reporting group title | Reference product |
| Reporting group description: - | |
| Reporting group title | Vehicle |
| Reporting group description: - | |
| Reporting group title | Test - Follow up |
| Reporting group description: - | |
| Reporting group title | Reference Follow up |
| Reporting group description: - | |
| Reporting group title | Vehicle Follow up |
| Reporting group description: - | |

### Primary: Primary endpoint

| | |
|---|---|
| End point title | Primary endpoint |

End point description:

The primary endpoint of the study was the clinical success rate at the end of treatment (Day 14). The success rate was defined as clinical and mycological cure. Clinical cure is gained when the total score of the 4 clinical parameters is ≤ 1 on Day 14 and no further treatment is necessary. Mycological cure is specified as a fungal culture score of ≤ 1 (only single forms of Candida albicans).

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Initial examination to main examination (EOT, day 14)

| End point values | Test product | Reference product | Vehicle | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 105 | 114 | 106 | |
| Units: percentage | 26 | 49 | 28 | |

### Statistical analyses

| Statistical analysis title | Non-Inferiority |
|---|---|

Statistical analysis description:

The primary objective of this study was to show non-inferiority of the test product in comparison to the reference product. Non-inferiority was statistically proven if the lower limit of the two-sided 95% confidence interval (CI) was > -D, where Δ = 0.20 was the non-inferiority limit.

| | |
|---|---|
| Comparison groups | Test product v Reference product |

| | |
|---|---|
| Number of subjects included in analysis | 219 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Median difference (final values) |
| Point estimate | -18.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -31.41 |
| upper limit | -5.03 |

| **Statistical analysis title** | Superiority of test product to vehicle |
|---|---|

Statistical analysis description:

The analysis was intended to provide supportive evidence with regard to assay sensitivity.

| | |
|---|---|
| Comparison groups | Test product v Vehicle |
| Number of subjects included in analysis | 211 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 1 |
| Method | Fisher exact |

Notes:

[1] - Difference between success rates

| **Statistical analysis title** | Superiority of reference product to vehicle |
|---|---|

Statistical analysis description:

This analysis was intended to provide supportive evidence with regard to assay sensitivity.

| | |
|---|---|
| Comparison groups | Reference product v Vehicle |
| Number of subjects included in analysis | 220 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| P-value | < 0.05 |
| Method | Fisher exact |

Notes:

[2] - Difference between success rates

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: From baseline to the end of follow-up. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22 |

| Reporting groups | |
|---|---|
| Reporting group title | Test product |
| Reporting group description: - | |
| Reporting group title | Reference product |
| Reporting group description: - | |
| Reporting group title | Vehicle |
| Reporting group description: - | |

| Serious adverse events | Test product | Reference product | Vehicle |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 2 / 127 (1.57%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| 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 | | | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (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 |

Frequency threshold for reporting non-serious adverse events: 0.05 %

| **Non-serious adverse events** | Test product | Reference product | Vehicle |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 125 (14.40%) | 26 / 130 (20.00%) | 25 / 127 (19.69%) |
| General disorders and administration site conditions | | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 2 / 130 (1.54%) | 4 / 127 (3.15%) |
| occurrences (all) | 0 | 2 | 4 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal discomfort | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Throat tightness | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Body temperature increased | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 3 / 130 (2.31%) | 1 / 127 (0.79%) |
| occurrences (all) | 2 | 3 | 1 |
| Migraine | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 2 / 130 (1.54%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 2 / 130 (1.54%) | 1 / 127 (0.79%) |
| occurrences (all) | 1 | 2 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 1 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 2 / 130 (1.54%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspepsia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Faeces hard | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Glossodynia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Oesophageal pain | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral discomfort | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 2 / 130 (1.54%) | 0 / 127 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Dermatitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lichen sclerosus | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| rash | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 1 | 0 | 1 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Urinary hesitation | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 1 | 1 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Bronchitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 1 | 0 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal candidiasis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Gonococcal infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 130 (0.00%) | 0 / 127 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 130 (0.00%) | 1 / 127 (0.79%) |
| occurrences (all) | 0 | 0 | 1 |
| Urethritis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 130 (0.77%) | 0 / 127 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Viral infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 125 (0.80%)<br>1 | 0 / 130 (0.00%)<br>0 | 0 / 127 (0.00%)<br>0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

| |
|---|
| None |

Notes: