# Clinical trial results:
# A randomized, double-blind, placebo-controlled, multicenter, parallel group, dose-finding, pivotal, Phase 2b/3 study to evaluate the efficacy, safety, and tolerability of intravenous BYM338 at 52 weeks on physical function, muscle strength, and mobility and additional long-term safety up to 2 years in patients with sporadic inclusion body myositis

## Summary

| | |
|---|---|
| EudraCT number | 2013-000705-23 |
| Trial protocol | IT NL DE BE GB DK |
| Global end of trial date | 06 January 2016 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 31 May 2017 |
| First version publication date | 21 January 2017 |
| Version creation reason | • New data added to full data set<br>• Correction of full data set<br>Title updated and new data added to secondary end point (EP) #2 (LBM); description updated for secondary EP #4 (sIFA); and title and unit updated in EP#5 (Falls). |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CBYM338B2203 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01925209 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 | 06 January 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 January 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that at least one dose regimen of bimagrumab in ambulatory sporadic inclusion body myositis (sIBM) patients increased the distance traveled, as measured by change from baseline at Week 52 of the 6MWD test relative to placebo.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 26 September 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 42 |
| Country: Number of subjects enrolled | Belgium: 9 |
| Country: Number of subjects enrolled | Denmark: 14 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | United Kingdom: 29 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Japan: 20 |
| Country: Number of subjects enrolled | Netherlands: 18 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 94 |
| Worldwide total number of subjects | 251 |
| EEA total number of subjects | 94 |

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) | 75 |
| From 65 to 84 years | 175 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were randomized into one of the four treatment arms in a 1:1:1:1 ratio.

### Pre-assignment

Screening details:

The study included 4 epochs: screening (up to 28 days pre-treatment), treatment (from day 1 up to 52 weeks), treatment maintenance (from week 52 up to 104 weeks) and follow-up (28 days after last dose administration). The disposition data reported are for the treatment epoch.

### Period 1

| | |
|---|---|
| Period 1 title | Treatment Epoch (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** | BYM338/bimagrumab 10 mg/kg |

Arm description:

Participants received study medication with BYM338 at 10 mg/kg from Day 1 to Week 52 and up to Week 104, administered by intravenous (i.v.) infusion every 4 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bimagrumab |
| Investigational medicinal product code | BYM338 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received BYM338 at 10 mg/kg intravenous (i.v.) infusion every 4 weeks from Day 1 to Week 52, and up to Week 104.

| | |
|---|---|
| **Arm title** | BYM338/bimagrumab 3 mg/kg |

Arm description:

Participants received study medication with BYM338 at 3 mg/kg from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bimagrumab |
| Investigational medicinal product code | BYM338 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received BYM338 at 3 mg/kg i.v. infusion every 4 weeks from Day 1 to Week 52, and up to Week 104.

| | |
|---|---|
| **Arm title** | BYM338/bimagrumab 1 mg/kg |

Arm description:

Participants received study medication with BYM338 at 1 mg/kg from Day 1 to Week 52 and up to Week

104, administered by i.v. infusion every 4 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bimagrumab |
| Investigational medicinal product code | BYM338 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received BYM338 at 1 mg/kg i.v. infusion every 4 weeks from Day 1 to Week 52, and up to Week 104.

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Participants received matching placebo to BYM338 from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received matching placebo to BYM338 i.v. infusion every 4 weeks from Day 1 to Week 52, and up to Week 104.

| **Number of subjects in period 1** | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg |
|---|---|---|---|
| Started | 63 | 63 | 63 |
| Full Analysis Set | 63 | 63 | 63 |
| Completed | 54 | 55 | 56 |
| Not completed | 9 | 8 | 7 |
| Adverse event, serious fatal | 1 | - | - |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | 3 | 5 | 3 |
| Protocol deviation | - | - | 1 |
| Non-compliance with study treatment | - | - | - |
| Withdrawal by subject | 4 | 3 | 3 |

| **Number of subjects in period 1** | Placebo |
|---|---|
| Started | 62 |
| Full Analysis Set | 62 |
| Completed | 57 |
| Not completed | 5 |
| Adverse event, serious fatal | - |

| | |
|---|---|
| Physician decision | - |
| Adverse event, non-fatal | 1 |
| Protocol deviation | 1 |
| Non-compliance with study treatment | 1 |
| Withdrawal by subject | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BYM338/bimagrumab 10 mg/kg |

Reporting group description:

Participants received study medication with BYM338 at 10 mg/kg from Day 1 to Week 52 and up to Week 104, administered by intravenous (i.v.) infusion every 4 weeks.

| Reporting group title | BYM338/bimagrumab 3 mg/kg |
|---|---|

Reporting group description:

Participants received study medication with BYM338 at 3 mg/kg from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

| Reporting group title | BYM338/bimagrumab 1 mg/kg |
|---|---|

Reporting group description:

Participants received study medication with BYM338 at 1 mg/kg from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

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

Reporting group description:

Participants received matching placebo to BYM338 from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

| Reporting group values | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg |
|---|---|---|---|
| Number of subjects | 63 | 63 | 63 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 16 | 27 | 14 |
| From 65-84 years | 47 | 36 | 48 |
| 85 years and over | 0 | 0 | 1 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 68 | 66.5 | 69.4 |
| standard deviation | ± 7.93 | ± 8.72 | ± 7.91 |
| Gender, Male/Female<br>Units: Subjects | | | |
| Female | 22 | 21 | 23 |
| Male | 41 | 42 | 40 |

| Reporting group values | Placebo | Total | |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Number of subjects | 62 | 251 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 18 | 75 | |
| From 65-84 years | 44 | 175 | |
| 85 years and over | 0 | 1 | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 68.4 | | |
| standard deviation | ± 8.12 | - | |
| Gender, Male/Female<br>Units: Subjects | | | |
| Female | 23 | 89 | |
| Male | 39 | 162 | |

## End points

### End points reporting groups

| Reporting group title | BYM338/bimagrumab 10 mg/kg |
|---|---|

Reporting group description:

Participants received study medication with BYM338 at 10 mg/kg from Day 1 to Week 52 and up to Week 104, administered by intravenous (i.v.) infusion every 4 weeks.

| Reporting group title | BYM338/bimagrumab 3 mg/kg |
|---|---|

Reporting group description:

Participants received study medication with BYM338 at 3 mg/kg from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

| Reporting group title | BYM338/bimagrumab 1 mg/kg |
|---|---|

Reporting group description:

Participants received study medication with BYM338 at 1 mg/kg from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

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

Reporting group description:

Participants received matching placebo to BYM338 from Day 1 to Week 52 and up to Week 104, administered by i.v. infusion every 4 weeks.

### Primary: Change from Baseline in 6 Minute Walking Distance (6MWD) Test at week 52

| End point title | Change from Baseline in 6 Minute Walking Distance (6MWD) Test at week 52 |
|---|---|

End point description:

The 6MWD test measured the distance (in meters) that a participant walked in a 6 minute timeframe. A positive change from baseline indicates improvement.

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

End point timeframe:

Baseline, Week 52

| End point values | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 63 | 63 | 62 |
| Units: meters | | | | |
| least squares mean (standard error) | 8.63 (± 10.934) | 9.63 (± 10.77) | -10.27 (± 10.718) | -8.96 (± 10.765) |

**Statistical analyses**

| **Statistical analysis title** | Change from Baseline in 6MWD at week 52 |
|---|---|
| Comparison groups | BYM338/bimagrumab 10 mg/kg v Placebo |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.221 |
| Method | mixed model repeated measures |
| Parameter estimate | Mean difference (net) |
| Point estimate | 17.59 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -19.63 |
| upper limit | 54.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 14.331 |

| **Statistical analysis title** | Change from Baseline in 6MWD at week 52 |
|---|---|
| Comparison groups | BYM338/bimagrumab 3 mg/kg v Placebo |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1909 |
| Method | mixed model repeated measure |
| Parameter estimate | Mean difference (net) |
| Point estimate | 18.59 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -18.21 |
| upper limit | 55.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 14.176 |

| **Statistical analysis title** | Change from Baseline in 6MWD at week 52 |
|---|---|
| Comparison groups | BYM338/bimagrumab 1 mg/kg v Placebo |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.9263 |
| Method | mixed models repeated measures |
| Parameter estimate | Mean difference (net) |
| Point estimate | -1.31 |

| | |
|---|---|
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -37.97 |
| upper limit | 35.36 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 14.121 |

## Secondary: Estimated within treatment group lean body mass (LBM) ratio at week 52

| | |
|---|---|
| End point title | Estimated within treatment group lean body mass (LBM) ratio at week 52 |

End point description:

LBM was measured via dual energy x-ray absorptiometry (DXA) and calculated as (LBM at Week 52/LBM at baseline)*100 . A positive change from baseline indicates improvement.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Week 52

| End point values | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 62 | 61 | 63 | 61 |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 102.8 (101.4 to 104.2) | 100.4 (99.1 to 101.8) | 98.3 (97 to 99.6) | 97.2 (95.9 to 98.5) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in quadriceps Quantitative Muscle Testing (QMT) on the right side at week 52

| | |
|---|---|
| End point title | Change from Baseline in quadriceps Quantitative Muscle Testing (QMT) on the right side at week 52 |

End point description:

Quadriceps muscle strength was measured by portable fixed dynamometry (PFD) on the right side. A negative change from baseline indicates deterioration.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Week 52

| End point values | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 60 | 63 | 63 | 61 |
| Units: newtons | | | | |
| least squares mean (standard error) | -12.44 (± 6.021) | -20.36 (± 5.843) | -14.89 (± 5.828) | -16.48 (± 5.83) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in sIBM functional assessment (sIFA) at week 52

| End point title | Change from baseline in sIBM functional assessment (sIFA) at week 52 |
|---|---|

End point description:

Self-reported physical function was assessed by a newly developed patient reported outcome named sporadic inclusion body myositis (sIBM) functional assessment (sIFA). The sIFA consists of 11 items scored on an 11 point numerical rating scale from 0 (no difficulty) to 10 (unable to do) across 3 domains: upper body functioning, lower body functioning and general functioning. Participants completed the assessment where the recall period was the past week prior to completing the patient reported outcome (PRO). The total score on the sIFA scale ranges from 0 (minimum) to 110 (maximum). Higher values represent a worse outcome. A positive change from baseline indicates deterioration.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 52

| End point values | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 61 | 63 | 60 | 61 |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 1.74 (± 1.915) | 3.56 (± 1.876) | 6.12 (± 1.899) | 6.85 (± 1.895) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Estimated annual number of falls per participant within treatment group

| End point title | Estimated annual number of falls per participant within treatment group |
|---|---|

End point description:

Participants documented any fall occurrences in a paper diary during the study.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 52

| **End point values** | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 63 | 63 | 63 | 62 |
| Units: Annual number of falls per participant | | | | |
| number (not applicable) | 4.33 | 4.02 | 4.7 | 5.13 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Short Physical Performance Battery (SPPB) score at week 52

| End point title | Change from Baseline in Short Physical Performance Battery (SPPB) score at week 52 |
|---|---|

End point description:

The SPPB evaluated lower extremities function by testing gait speed, ability to keep standing balance and time to rise from a chair five times. The sub-score for each test ranged from 0 to 4. The summary score, which was a summation of scores from the 3 tests, ranged from 0 to 12. An increase in score indicates improvement in physical performance. A negative change from baseline indicates deterioration.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 52

| **End point values** | BYM338/bimagrumab 10 mg/kg | BYM338/bimagrumab 3 mg/kg | BYM338/bimagrumab 1 mg/kg | Placebo |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 62 | 63 | 63 | 62 |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 0 (± 0.24) | 0 (± 0.23) | -0.5 (± 0.23) | -0.5 (± 0.23) |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | BYM338 10 mg/kg |
| Reporting group description: | |
| BYM338 10 mg/kg | |
| Reporting group title | BYM338 3 mg/kg |
| Reporting group description: | |
| BYM338 3 mg/kg | |
| Reporting group title | BYM338 1 mg/kg |
| Reporting group description: | |
| BYM338 1 mg/kg | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo | |

| Serious adverse events | BYM338 10 mg/kg | BYM338 3 mg/kg | BYM338 1 mg/kg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 63 (33.33%) | 11 / 63 (17.46%) | 18 / 63 (28.57%) |
| number of deaths (all causes) | 1 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BASAL CELL CARCINOMA | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 3 / 63 (4.76%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG ADENOCARCINOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 / 1 |
| SQUAMOUS CELL CARCINOMA | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 2 / 63 (3.17%) | 2 / 63 (3.17%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SQUAMOUS CELL CARCINOMA OF SKIN | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Vascular disorders | | | |
| AORTIC ANEURYSM | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ISCHAEMIA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| INJURY ASSOCIATED WITH DEVICE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ASPIRATION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| PNEUMONIA ASPIRATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| SUICIDE ATTEMPT | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| Injury, poisoning and procedural complications | | | |
| ANKLE FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| CARBON MONOXIDE POISONING | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| CERVICAL VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| ENDOTRACHEAL INTUBATION COMPLICATION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| EYE INJURY | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| FACIAL BONES FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| FALL | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 2 / 63 (3.17%) | 4 / 63 (6.35%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 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 |
| FIBULA FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FOOT FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAND FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| HIP FRACTURE | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| INTENTIONAL OVERDOSE | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 / 1 | 0 / 0 | 0 / 0 |
| LACERATION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| PATELLA FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL CORD INJURY CERVICAL | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| THORACIC VERTEBRAL FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 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 |
| TIBIA FRACTURE | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 2 / 63 (3.17%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRAUMATIC HAEMATOMA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| VASCULAR PSEUDOANEURYSM | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| WRIST FRACTURE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK SECOND DEGREE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 / 1 | 0 / 0 | 0 / 0 |
| PALPITATIONS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| CAROTID ARTERY STENOSIS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| SYNCOPE | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSIENT GLOBAL AMNESIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| TRANSIENT ISCHAEMIC ATTACK | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 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 / 63 (0.00%) | 0 / 63 (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 |
| IRON DEFICIENCY ANAEMIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Eye disorders | | | |
| RETINAL ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| ABDOMINAL HERNIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHOEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 63 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| INGUINAL HERNIA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOLVULUS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 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 / 63 (0.00%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RASH PRURITIC | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Renal and urinary disorders | | | |
| BLADDER MASS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| URINARY RETENTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 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 |
| VERTEBRAL FORAMINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| Infections and infestations | | | |
| DIVERTICULITIS | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 63 (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 |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 |
| STREPTOCOCCAL BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (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 | 1 / 63 (1.59%) | 0 / 63 (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 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 63 (1.59%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Placebo | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 20 / 62 (32.26%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| BASAL CELL CARCINOMA | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LUNG ADENOCARCINOMA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SQUAMOUS CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SQUAMOUS CELL CARCINOMA OF SKIN | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| AORTIC ANEURYSM | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PERIPHERAL ISCHAEMIA | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| INJURY ASSOCIATED WITH DEVICE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| ASPIRATION | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA ASPIRATION | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PULMONARY EMBOLISM | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| DEPRESSION | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| SUICIDE ATTEMPT | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| ANKLE FRACTURE | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CARBON MONOXIDE POISONING | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CERVICAL VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENDOTRACHEAL INTUBATION COMPLICATION | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| EYE INJURY | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FACIAL BONES FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FALL | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FEMUR FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FIBULA FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FOOT FRACTURE | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HAND FRACTURE | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HIP FRACTURE | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INTENTIONAL OVERDOSE | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LACERATION | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PATELLA FRACTURE | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| SPINAL CORD INJURY CERVICAL | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| THORACIC VERTEBRAL FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| TIBIA FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| TRAUMATIC HAEMATOMA | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| VASCULAR PSEUDOANEURYSM | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| WRIST FRACTURE | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| ACUTE 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 | | | |
| ATRIAL FIBRILLATION | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ATRIOVENTRICULAR BLOCK | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ATRIOVENTRICULAR BLOCK SECOND DEGREE | | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| 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 | | | |
| PALPITATIONS | | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |

| | | | |
|---|---|---|---|
| CAROTID ARTERY STENOSIS | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PRESYNCOPE | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TRANSIENT GLOBAL AMNESIA | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TRANSIENT ISCHAEMIC ATTACK | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| IRON DEFICIENCY ANAEMIA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Eye disorders | | | |
| RETINAL ARTERY OCCLUSION | | | |
| 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 | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ABDOMINAL HERNIA | | | |
| 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 UPPER | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INGUINAL HERNIA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VOLVULUS | | | |
| 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 | | |
| RASH PRURITIC | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| BLADDER MASS | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY RETENTION | | | |
| 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 | | |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VERTEBRAL FORAMINAL STENOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| DIVERTICULITIS | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| STREPTOCOCCAL BACTERAEMIA | | | |
| 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 | | |
| HYPONATRAEMIA | | | |
| 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: 5 %

| **Non-serious adverse events** | BYM338 10 mg/kg | BYM338 3 mg/kg | BYM338 1 mg/kg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 63 / 63 (100.00%) | 63 / 63 (100.00%) | 63 / 63 (100.00%) |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 63 (3.17%) | 7 / 63 (11.11%) |
| occurrences (all) | 1 | 2 | 9 |
| HYPERTENSION | | | |
| subjects affected / exposed | 7 / 63 (11.11%) | 7 / 63 (11.11%) | 5 / 63 (7.94%) |
| occurrences (all) | 7 | 7 | 6 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 3 / 63 (4.76%) | 4 / 63 (6.35%) |
| occurrences (all) | 1 | 3 | 4 |
| FATIGUE | | | |
| subjects affected / exposed | 9 / 63 (14.29%) | 4 / 63 (6.35%) | 14 / 63 (22.22%) |
| occurrences (all) | 10 | 4 | 28 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 9 / 63 (14.29%) | 9 / 63 (14.29%) |
| occurrences (all) | 6 | 11 | 9 |
| PYREXIA | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 1 / 63 (1.59%) | 3 / 63 (4.76%) |
| occurrences (all) | 3 | 1 | 4 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 3 / 63 (4.76%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 3 | 4 |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 2 | 0 | 1 |
| RHINORRHOEA | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 3 / 63 (4.76%) | 5 / 63 (7.94%) |
| occurrences (all) | 4 | 3 | 5 |
| Psychiatric disorders | | | |
| ANXIETY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 63 (3.17%) | 1 / 63 (1.59%) |
| occurrences (all) | 4 | 2 | 1 |
| DEPRESSED MOOD | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 1 / 63 (1.59%) | 0 / 63 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 1 / 63 (1.59%) | 5 / 63 (7.94%) |
| occurrences (all) | 4 | 1 | 5 |
| INSOMNIA | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 0 / 63 (0.00%) | 2 / 63 (3.17%) |
| occurrences (all) | 6 | 0 | 2 |
| Investigations | | | |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 5 / 63 (7.94%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 5 | 4 |
| VITAMIN D DECREASED | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 63 (3.17%) | 3 / 63 (4.76%) |
| occurrences (all) | 4 | 3 | 3 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 9 / 63 (14.29%) | 4 / 63 (6.35%) | 8 / 63 (12.70%) |
| occurrences (all) | 9 | 4 | 8 |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 14 / 63 (22.22%) | 23 / 63 (36.51%) | 22 / 63 (34.92%) |
| occurrences (all) | 53 | 34 | 37 |
| FALL | | | |
| subjects affected / exposed | 47 / 63 (74.60%) | 55 / 63 (87.30%) | 54 / 63 (85.71%) |
| occurrences (all) | 281 | 286 | 294 |
| FOOT FRACTURE | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 3 / 63 (4.76%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 4 | 4 |
| HEAD INJURY | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 4 / 63 (6.35%) | 3 / 63 (4.76%) |
| occurrences (all) | 4 | 4 | 3 |
| INJURY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 63 (6.35%) | 0 / 63 (0.00%) | 7 / 63 (11.11%) |
| occurrences (all) | 8 | 0 | 9 |
| JOINT INJURY | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 3 / 63 (4.76%) | 6 / 63 (9.52%) |
| occurrences (all) | 13 | 4 | 6 |
| LACERATION | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 5 / 63 (7.94%) | 12 / 63 (19.05%) |
| occurrences (all) | 7 | 5 | 14 |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 7 / 63 (11.11%) | 10 / 63 (15.87%) | 9 / 63 (14.29%) |
| occurrences (all) | 8 | 14 | 12 |
| LIMB INJURY | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 7 / 63 (11.11%) | 2 / 63 (3.17%) |
| occurrences (all) | 6 | 10 | 3 |
| SKIN ABRASION | | | |
| subjects affected / exposed | 14 / 63 (22.22%) | 14 / 63 (22.22%) | 14 / 63 (22.22%) |
| occurrences (all) | 28 | 16 | 23 |
| SOFT TISSUE INJURY | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 5 / 63 (7.94%) | 1 / 63 (1.59%) |
| occurrences (all) | 3 | 13 | 3 |
| Nervous system disorders | | | |
| DIZZINESS | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 10 / 63 (15.87%) | 6 / 63 (9.52%) |
| occurrences (all) | 7 | 13 | 7 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 1 / 63 (1.59%) | 0 / 63 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| HEADACHE | | | |
| subjects affected / exposed | 12 / 63 (19.05%) | 4 / 63 (6.35%) | 14 / 63 (22.22%) |
| occurrences (all) | 21 | 7 | 23 |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 1 / 63 (1.59%) | 3 / 63 (4.76%) |
| occurrences (all) | 2 | 1 | 3 |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 63 (4.76%) | 6 / 63 (9.52%) | 0 / 63 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| PARAESTHESIA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 63 (3.17%) | 2 / 63 (3.17%) |
| occurrences (all) | 0 | 2 | 2 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 3 / 63 (4.76%) | 0 / 63 (0.00%) |
| occurrences (all) | 5 | 3 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 4 / 63 (6.35%) | 0 / 63 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 6 / 63 (9.52%) | 1 / 63 (1.59%) |
| occurrences (all) | 3 | 8 | 1 |
| CONSTIPATION | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 3 / 63 (4.76%) | 6 / 63 (9.52%) |
| occurrences (all) | 6 | 3 | 6 |
| DIARRHOEA | | | |
| subjects affected / exposed | 32 / 63 (50.79%) | 28 / 63 (44.44%) | 20 / 63 (31.75%) |
| occurrences (all) | 56 | 65 | 50 |
| DRY MOUTH | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 1 / 63 (1.59%) | 3 / 63 (4.76%) |
| occurrences (all) | 5 | 1 | 4 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 63 (6.35%) | 1 / 63 (1.59%) |
| occurrences (all) | 6 | 4 | 1 |
| NAUSEA | | | |
| subjects affected / exposed | 11 / 63 (17.46%) | 4 / 63 (6.35%) | 9 / 63 (14.29%) |
| occurrences (all) | 13 | 5 | 11 |
| VOMITING | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 1 / 63 (1.59%) | 2 / 63 (3.17%) |
| occurrences (all) | 4 | 1 | 2 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| ACNE | | | |
| subjects affected / exposed | 12 / 63 (19.05%) | 19 / 63 (30.16%) | 8 / 63 (12.70%) |
| occurrences (all) | 15 | 33 | 10 |
| DRY SKIN | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 63 (3.17%) | 1 / 63 (1.59%) |
| occurrences (all) | 1 | 2 | 1 |
| PRURITUS | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 6 / 63 (9.52%) | 6 / 63 (9.52%) |
| occurrences (all) | 7 | 6 | 6 |
| RASH | | | |
| subjects affected / exposed | 13 / 63 (20.63%) | 8 / 63 (12.70%) | 9 / 63 (14.29%) |
| occurrences (all) | 17 | 15 | 10 |
| ROSACEA | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 4 / 63 (6.35%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 15 / 63 (23.81%) | 14 / 63 (22.22%) | 19 / 63 (30.16%) |
| occurrences (all) | 20 | 24 | 36 |
| BACK PAIN | | | |
| subjects affected / exposed | 10 / 63 (15.87%) | 8 / 63 (12.70%) | 14 / 63 (22.22%) |
| occurrences (all) | 10 | 8 | 17 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 63 (6.35%) | 1 / 63 (1.59%) |
| occurrences (all) | 6 | 4 | 2 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 32 / 63 (50.79%) | 43 / 63 (68.25%) | 25 / 63 (39.68%) |
| occurrences (all) | 54 | 69 | 33 |
| MUSCLE TWITCHING | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 4 / 63 (6.35%) | 2 / 63 (3.17%) |
| occurrences (all) | 3 | 6 | 2 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 4 / 63 (6.35%) | 3 / 63 (4.76%) |
| occurrences (all) | 2 | 4 | 3 |
| MUSCULOSKELETAL PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 63 (6.35%) | 7 / 63 (11.11%) |
| occurrences (all) | 5 | 5 | 10 |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 0 / 63 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 5 | 0 | 1 |
| MYALGIA | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 11 / 63 (17.46%) | 7 / 63 (11.11%) |
| occurrences (all) | 5 | 13 | 10 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 63 (6.35%) | 13 / 63 (20.63%) |
| occurrences (all) | 5 | 5 | 26 |
| Infections and infestations | | | |
| FOLLICULITIS | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 63 (3.17%) | 0 / 63 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 4 / 63 (6.35%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 5 | 4 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 11 / 63 (17.46%) | 9 / 63 (14.29%) |
| occurrences (all) | 8 | 11 | 13 |
| RHINITIS | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 63 (1.59%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 2 | 1 |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 4 / 63 (6.35%) | 1 / 63 (1.59%) |
| occurrences (all) | 3 | 4 | 1 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 11 / 63 (17.46%) | 11 / 63 (17.46%) | 14 / 63 (22.22%) |
| occurrences (all) | 13 | 14 | 19 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 4 / 63 (6.35%) | 2 / 63 (3.17%) |
| occurrences (all) | 4 | 7 | 4 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| DECREASED APPETITE | | | |
| subjects affected / exposed | 10 / 63 (15.87%) | 3 / 63 (4.76%) | 3 / 63 (4.76%) |
| occurrences (all) | 10 | 3 | 3 |
| GOUT | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 63 (0.00%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 0 | 6 |
| HYPERCHOLESTEROLAEMIA | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 4 / 63 (6.35%) | 2 / 63 (3.17%) |
| occurrences (all) | 2 | 4 | 2 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 63 (3.17%) | 0 / 63 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| VITAMIN D DEFICIENCY | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 12 / 63 (19.05%) | 3 / 63 (4.76%) |
| occurrences (all) | 7 | 13 | 3 |

| **Non-serious adverse events** | Placebo | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 61 / 62 (98.39%) | | |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 3 | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 9 / 62 (14.52%) | | |
| occurrences (all) | 12 | | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 6 / 62 (9.68%) | | |
| occurrences (all) | 6 | | |
| FATIGUE | | | |
| subjects affected / exposed | 7 / 62 (11.29%) | | |
| occurrences (all) | 8 | | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 7 / 62 (11.29%) | | |
| occurrences (all) | 8 | | |
| PYREXIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 16 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | | |
| occurrences (all) | 10 | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 4 | | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| DEPRESSED MOOD | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| INSOMNIA | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| VITAMIN D DECREASED | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 3 | | |
| Injury, poisoning and procedural | | | |

| | | | |
|---|---|---|---|
| complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 22 / 62 (35.48%) | | |
| occurrences (all) | 34 | | |
| FALL | | | |
| subjects affected / exposed | 52 / 62 (83.87%) | | |
| occurrences (all) | 356 | | |
| FOOT FRACTURE | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 4 | | |
| HEAD INJURY | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 6 | | |
| INJURY | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 4 | | |
| JOINT INJURY | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| LACERATION | | | |
| subjects affected / exposed | 9 / 62 (14.52%) | | |
| occurrences (all) | 15 | | |
| LIGAMENT SPRAIN | | | |
| subjects affected / exposed | 10 / 62 (16.13%) | | |
| occurrences (all) | 14 | | |
| LIMB INJURY | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | | |
| occurrences (all) | 10 | | |
| SKIN ABRASION | | | |
| subjects affected / exposed | 17 / 62 (27.42%) | | |
| occurrences (all) | 35 | | |
| SOFT TISSUE INJURY | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| DIZZINESS | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | | |
| occurrences (all) | 11 | | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| HEADACHE | | | |
| subjects affected / exposed | 9 / 62 (14.52%) | | |
| occurrences (all) | 15 | | |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 6 | | |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| PARAESTHESIA | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 3 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 11 / 62 (17.74%) | | |
| occurrences (all) | 30 | | |
| DRY MOUTH | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 4 | | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| NAUSEA | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| VOMITING | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 3 | | |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 6 / 62 (9.68%) | | |
| occurrences (all) | 6 | | |
| DRY SKIN | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | | |
| occurrences (all) | 5 | | |
| PRURITUS | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| RASH | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | | |
| occurrences (all) | 10 | | |
| ROSACEA | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 15 / 62 (24.19%) | | |
| occurrences (all) | 29 | | |
| BACK PAIN | | | |
| subjects affected / exposed | 9 / 62 (14.52%) | | |
| occurrences (all) | 13 | | |
| JOINT SWELLING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 62 (9.68%) | | |
| occurrences (all) | 6 | | |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 13 / 62 (20.97%) | | |
| occurrences (all) | 17 | | |
| MUSCLE TWITCHING | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 6 | | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | | |
| occurrences (all) | 3 | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 4 | | |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| MYALGIA | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | | |
| occurrences (all) | 12 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 7 / 62 (11.29%) | | |
| occurrences (all) | 9 | | |
| Infections and infestations | | | |
| FOLLICULITIS | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | | |
| occurrences (all) | 1 | | |
| INFLUENZA | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | | |
| occurrences (all) | 2 | | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 6 / 62 (9.68%) | | |
| occurrences (all) | 6 | | |
| RHINITIS | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 5 | | |

| | | | |
|---|---|---|---|
| SINUSITIS<br>subjects affected / exposed<br>occurrences (all) | 4 / 62 (6.45%)<br>6 | | |
| UPPER RESPIRATORY TRACT INFECTION<br>subjects affected / exposed<br>occurrences (all) | 10 / 62 (16.13%)<br>16 | | |
| URINARY TRACT INFECTION<br>subjects affected / exposed<br>occurrences (all) | 4 / 62 (6.45%)<br>4 | | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1 | | |
| GOUT<br>subjects affected / exposed<br>occurrences (all) | 2 / 62 (3.23%)<br>5 | | |
| HYPERCHOLESTEROLAEMIA<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1 | | |
| HYPOMAGNESAEMIA<br>subjects affected / exposed<br>occurrences (all) | 0 / 62 (0.00%)<br>0 | | |
| VITAMIN D DEFICIENCY<br>subjects affected / exposed<br>occurrences (all) | 11 / 62 (17.74%)<br>12 | | |

## 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

None reported