# Clinical trial results:
# Randomised, double-blind, placebo-controlled, clinical study to evaluate the effect of opicapone 50 mg on Parkinson's disease patients with end-of-dose motor fluctuations and associated pain.

## Summary

| | |
|---|---|
| EudraCT number | 2020-001175-32 |
| Trial protocol | GB PT IT CZ PL |
| Global end of trial date | 16 February 2024 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 30 May 2025 |
| First version publication date | 30 May 2025 |
| Summary attachment (see zip file) | BIA-91067-404_CTR Synopsis (BIA-91067-404_CTR Synopsis.pdf) |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | BIA-91067-404 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04986982 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Bial - Portela & Ca, S.A. |
| Sponsor organisation address | À Av. da Siderurgia Nacional, Trofa, Portugal, 4745-457 |
| Public contact | Ruben Arnelas, Bial - Portela & Ca, S.A., +351 229866100, clinical.trials@bial.com |
| Scientific contact | Responsible of Clinical Development, Bial - Portela & Ca, S.A., +351 229866100, clinical.trials@bial.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 | 21 May 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 February 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the efficacy of opicapone 50 mg when administered with the existing treatment of L-DOPA plus a DDCI, in PD patients with end-of-dose motor fluctuations and associated pain.

Protection of trial subjects:

This study was performed in neurological centres and conducted in compliance with the study protocol, by the study personnel, who were qualified by education, training, and experienced in their roles. The patients were closely monitored during the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 25 February 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 28 |
| Country: Number of subjects enrolled | Czechia: 26 |
| Country: Number of subjects enrolled | Portugal: 20 |
| Country: Number of subjects enrolled | Spain: 16 |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Country: Number of subjects enrolled | Germany: 8 |
| Country: Number of subjects enrolled | Italy: 10 |
| Worldwide total number of subjects | 127 |
| EEA total number of subjects | 108 |

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) | 52 |
| From 65 to 84 years | 74 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

The recruitment was terminated before reaching the estimated number of randomised patients. However, this had no impact on the analysis of data since the drop-out rate was less than 15% and thus the planned number of evaluable patients was reached. A total of 19 patients prematurely terminated the study.

### Pre-assignment

Screening details:

A total of 144 patients were enrolled at 44 active sites in Europe. Of these, 127 patients were randomised and received at least 1 dose of IP. A total of 122 patients met the criteria for the Full Analysis Set including 59 opicapone 50 mg patients and 63 placebo patients.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group A - Opicapone |

Arm description:

Opicapone (BIA 9-1067) 50 mg hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Opicapone |
| Investigational medicinal product code | BIA 9-1067 |
| Other name | Ongentys |
| Pharmaceutical forms | Oral suspension, Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI.

| | |
|---|---|
| **Arm title** | Group B - Placebo |

Arm description:

Matching placebo hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI

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

Dosage and administration details:

Matching placebo hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI

| **Number of subjects in period 1** | Group A - Opicapone | Group B - Placebo |
|---|---|---|
| Started | 64 | 63 |
| Completed | 53 | 55 |
| Not completed | 11 | 8 |
| Consent withdrawn by subject | 3 | 1 |
| Adverse event, non-fatal | 4 | 4 |
| Ineligibility | 3 | - |
| Sponsor's discretion | 1 | - |
| Lost to follow-up | - | 1 |
| Lack of efficacy | - | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Group A - Opicapone |
| Reporting group description: | |
| Opicapone (BIA 9-1067) 50 mg hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI | |
| Reporting group title | Group B - Placebo |
| Reporting group description: | |
| Matching placebo hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI | |

| Reporting group values | Group A - Opicapone | Group B - Placebo | Total |
|---|---|---|---|
| Number of subjects | 64 | 63 | 127 |
| 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) | 23 | 29 | 52 |
| From 65-84 years | 40 | 34 | 74 |
| 85 years and over | 1 | 0 | 1 |
| Age continuous<br>Units: years | | | |
| median | 67.0 | 65 | |
| standard deviation | ± 9.14 | ± 9.39 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 31 | 31 | 62 |
| Male | 33 | 32 | 65 |
| Race<br>Units: Subjects | | | |
| White | 64 | 62 | 126 |
| Black or African American | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| American Indian or Alaska Native | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Unknown | 0 | 0 | 0 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Group A - Opicapone |
| Reporting group description: | |
| Opicapone (BIA 9-1067) 50 mg hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI | |
| Reporting group title | Group B - Placebo |
| Reporting group description: | |
| Matching placebo hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI | |

### Primary: Change From Baseline in Domain 3 (Fluctuation-related Pain) of KING's PARKINSON's DISEASE PAIN SCALE (KPPS)

| | |
|---|---|
| End point title | Change From Baseline in Domain 3 (Fluctuation-related Pain) of KING's PARKINSON's DISEASE PAIN SCALE (KPPS) |
| End point description: | |
| The KING's PARKINSON's DISEASE PAIN SCALE (KPPS) evaluates the burden (global and bedside) and characterises various phenotypes of pain in Parkinson's disease. The investigator will complete the questionnaire by interviewing the patient about seven domains and answering to 14 items. The questionnaire will be fill out on Visit 1, Visit 2b/Baseline, Visit 4, Visit 5 and Visit 6/EDV Domain 3 assesses fluctuation-related pain (score range: 0 - 36). Higher score values indicate higher levels of pain. | |
| End point type | Primary |
| End point timeframe: | |
| The questionnaire will be fill out on Visit 1 (Day -7 ±2), Visit 2b/Baseline (Day 1), Visit 4 (Day 29 (±2)), Visit 5 (Day 85 (±4)) and Visit 6/Early Discontinuation Visit (EDV) (Day 169 (±4)) - Up to 24 weeks | |

| End point values | Group A - Opicapone | Group B - Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 63 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Visit 1 (Day -7 ±2) | 17.2 (± 5.72) | 16.7 (± 5.18) | | |
| Visit 2b (Day 1) | 17.1 (± 5.58) | 16.9 (± 5.20) | | |
| Baseline (Day 1) | 17.1 (± 5.58) | 16.9 (± 5.20) | | |
| Visit 4 (Day 29 (±2)) - Observed Value | 10.5 (± 7.92) | 11.0 (± 7.51) | | |
| Visit 4 (Day 29 (±2)) - Change from Baseline | -6.6 (± 7.28) | -5.9 (± 6.02) | | |
| Visit 5 (Day 85 (±4)) - Observed Value | 8.3 (± 7.27) | 9.3 (± 5.73) | | |
| Visit 5 (Day 85 (±4)) - Change from Baseline | -8.7 (± 6.68) | -7.6 (± 6.13) | | |
| Visit 6 (Day 169 (±4)) - Observed Value | 8.4 (± 6.93) | 7.5 (± 6.48) | | |
| Visit 6 (Day 169 (±4)) - Change from Baseline | -8.8 (± 6.85) | -9.3 (± 6.24) | | |

## Statistical analyses

| **Statistical analysis title** | Change from baseline in Domain 3 of KPPS |
|---|---|

Statistical analysis description:

The King’s Parkinson’s Disease Pain Scale (KPPS) evaluates the burden (global and bedside) and characterises various phenotypes of pain in PD. Its seven domains include 14 items, each item scored by severity (0-3) multiplied by frequency (0-4), resulting in subscores of 0 to 12. The total possible KPPS score (0 to 168) represents the symptomatic burden by pain. The questionnaire will be fill out on Visit 1, Visit 2b, Visit 4, Visit 5 and Visit 6/EDV.

| | |
|---|---|
| Comparison groups | Group B - Placebo v Group A - Opicapone |
| Number of subjects included in analysis | 122 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.794 |
| Method | Mixed models analysis |
| Confidence interval | |
| sides | 2-sided |
| lower limit | -1.96 |
| upper limit | 2.55 |
| Variability estimate | Standard deviation |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The period of monitored/assessed for the collection of AEs were through study completion, about 3 years.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

### Reporting groups

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

Reporting group description:

Opicapone 50 mg: Opicapone (BIA 9-1067) 50 mg hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI

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

Reporting group description:

Placebo: Matching placebo hard capsules. Oral administration, once daily, at least 1 hour before or after the last daily dose of L-dopa/DDCI

| Serious adverse events | Opicapone 50 mg | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 64 (6.25%) | 2 / 63 (3.17%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | Opicapone 50 mg | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 64 (62.50%) | 36 / 63 (57.14%) | |
| Vascular disorders | | | |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 63 (1.59%) | |
| occurrences (all) | 2 | 1 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 5 / 64 (7.81%) | 3 / 63 (4.76%) | |
| occurrences (all) | 6 | 3 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 2 / 63 (3.17%) | |
| occurrences (all) | 2 | 2 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Application site irritation | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Reproductive system and breast disorders | | | |

| | | | |
|---|---|---|---|
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus genital | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Anxiety | | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 2 / 63 (3.17%) | |
| occurrences (all) | 6 | 3 | |
| Insomnia | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 3 / 63 (4.76%) | |
| occurrences (all) | 3 | 3 | |
| Depression | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 1 / 63 (1.59%) | |
| occurrences (all) | 3 | 1 | |
| Hallucination, visual | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Abnormal dreams | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Bruxism | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Delirium | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Delusion | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Depressed mood | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hallucinations, mixed | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Illusion | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Impulse-control disorder | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Irritability | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mixed anxiety and depressive disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Mood altered | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nightmare | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Obsessive-compulsive disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Terminal insomnia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Blood pressure decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Body temperature increased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 3 / 63 (4.76%) | |
| occurrences (all) | 7 | 3 | |
| Skin abrasion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Chest injury | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiomegaly | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Dyskinesia | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 4 / 63 (6.35%) | |
| occurrences (all) | 3 | 4 | |
| Headache | | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 3 / 63 (4.76%) | |
| occurrences (all) | 4 | 3 | |
| Parkinson's disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 64 (4.69%) | 3 / 63 (4.76%) | |
| occurrences (all) | 3 | 3 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 3 / 63 (4.76%) | |
| occurrences (all) | 1 | 4 | |
| On and off phenomenon | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 2 / 63 (3.17%) | |
| occurrences (all) | 2 | 2 | |
| Sciatica | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Bradykinesia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dystonia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Freezing phenomenon | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Poor quality sleep | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Taste disorder | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tension headache | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 63 (1.59%) | |
| occurrences (all) | 2 | 2 | |
| Eye disorders | | | |
| Diplopia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 7 / 64 (10.94%) | 5 / 63 (7.94%) | |
| occurrences (all) | 8 | 5 | |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 64 (7.81%) | 1 / 63 (1.59%) | |
| occurrences (all) | 5 | 1 | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 63 (1.59%) | |
| occurrences (all) | 2 | 1 | |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 63 (3.17%) | |
| occurrences (all) | 0 | 2 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Oral discomfort | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Toothache | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Umbilical hernia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nocturia | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Renal cyst | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 2 / 63 (3.17%) | |
| occurrences (all) | 2 | 2 | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 2 / 63 (3.17%) | |
| occurrences (all) | 1 | 2 | |

| | | | |
|---|---|---|---|
| Back pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 3 / 63 (4.76%) | |
| occurrences (all) | 0 | 3 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Limb discomfort | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Mobility decreased | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tonsillitis bacterial | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 1 / 63 (1.59%) | |
| occurrences (all) | 2 | 1 | |
| Folate deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 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

None reported