Clinical trial results:
Efficacy and safety of ODM-104 compared to a standard combination (Stalevo); a randomised, double-blind, crossover proof-of-concept study in patients with Parkinson's disease and end-of-dose wearing-off.

Summary

EudraCT number	2015-004507-23
Trial protocol	LV DE HU FI
Global end of trial date	27 March 2018

Results information

Result version number	v1 (current)
This version publication date	03 April 2019
First version publication date	03 April 2019

Trial information

Trial identification

Sponsor protocol code	3112004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02764125
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orion Corporation Orion Pharma
Sponsor organisation address	Orionintie 1, Espoo, Finland, 02200
Public contact	clinicaltrials@orionpharma.com, Orion Corporation Orion Pharma, 358 0104261, clinicaltrials@orionpharma.com
Scientific contact	clinicaltrials@orionpharma.com, Orion Corporation Orion Pharma, 358 0104261, clinicaltrials@orionpharma.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	27 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 March 2018
Global end of trial reached?	Yes
Global end of trial date	27 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy and safety of ODM-104 in combination with modified release (MR) levodopa and 65 mg of carbidopa in the treatment of Parkinson's disease (PD) patients with end-of-dose wearing-off (motor
fluctuations) compared to active control (Stalevo).

Protection of trial subjects:

ECG and safety laboratory parameters were measured at screening, at each visit and at the end-of-study visit. Adverse events were followed from
the time that a study subject signed the IC form until the end-of-study visit (7-21 days after the last study treatment administration).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2016
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	Finland: 7
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Latvia: 18
Worldwide total number of subjects	84
EEA total number of subjects	84

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)	40
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Male and female patients with Parkinson's disease were recruited in four countries during the years 2016-2018.

Pre-assignment

Screening details:

Male or female patients with idiopathic PD, with end-of-dose wearingoff (motor fluctuations). Hoehn and Yahr stage 2-4 performed during the ON-state. At least 2 h of OFF-time on each day. Treatment with 4-8 daily doses of levodopa/AADC inhibitor, either combined or without entacapone. Age of 30 years or above.

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, Monitor, Data analyst

Blinding implementation details:

Double dummy technique was used.

Arms

Are arms mutually exclusive?	No
Arm title	ODM-104

Arm description:

ODM-104 100 mg, carbidopa 65 mg and levodopa according to subject's own individual levodopa dose.

Arm type	Experimental
Investigational medicinal product name	ODM-104 100 mg capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

100 mg of ODM-104 with 65 mg of carbidopa and levodopa (the dose depended on subject’s own individual levodopa dose) and
placebo for Stalevo. The daily dose of ODM-104 was 400 - 800 mg, levodopa 300 - 1200 mg and carbidopa 75 - 520 mg.

Arm title	Stalevo

Arm description:

Stalevo combination tablets containing levodopa/carbidopa/entacapone.

Arm type	Active comparator
Investigational medicinal product name	Stalevo tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Levodopa/carbidopa/entacapone combination (Stalevo) and placebo for ODM-104. The daily dose of levodopa was 300 - 1200 mg, carbidopa 75 - 520 mg and entacapone 800 - 1600 mg.

Number of subjects in period 1	ODM-104	Stalevo
Started	84	84
Completed	70	70
Not completed	14	14
Adverse event, non-fatal	8	8
Other	4	4
Personal reason	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	84	84	
Age categorical 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)	40	40	
From 65-84 years	44	44	
85 years and over	0	0	
Gender categorical Units: Subjects			
Females	31	31	
Males	53	53	

End points

End points reporting groups

Reporting group title	ODM-104
Reporting group description:	
ODM-104 100 mg, carbidopa 65 mg and levodopa according to subject's own individual levodopa dose.	
Reporting group title	Stalevo
Reporting group description:	
Stalevo combination tablets containing levodopa/carbidopa/entacapone.	

Primary: Mean change in OFF-time

End point title	Mean change in OFF-time
End point description:	
End point type	Primary
End point timeframe:	
The subjects recorded their PD status using the ON/OFF diary on 3 consecutive days before baseline and weeks 4 and 8 visits, after 4 weeks of each treatments.	

End point values	ODM-104	Stalevo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72[1]	73[2]		
Units: hour				
least squares mean (confidence interval 95%)	-1.0687 (-1.73 to -0.41)	-0.9644 (-1.62 to -0.31)		

Notes:

[1] - miTT population

[2] - miTT population

Statistical analyses

Statistical analysis title	Change from baseline in duration of daily OFF-time
Statistical analysis description:	
Analysed using an analysis of covariance (ANCOVA) model for crossover design.	
Comparison groups	ODM-104 v Stalevo
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7718
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.104

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.819
upper limit	0.61

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of the study treatment until the end-of-study visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	ODM-104
Reporting group description:	
ODM-104 100 mg, carbidopa 65 mg and levodopa according to subject's own individual levodopa dose.	
Reporting group title	Stalevo
Reporting group description:	
Stalevo combination tablets containing levodopa/carbidopa/entacapone.	

Serious adverse events	ODM-104	Stalevo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 81 (7.41%)	0 / 78 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastric neoplasm			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Localised infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	ODM-104	Stalevo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 81 (60.49%)	47 / 78 (60.26%)	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Hypotension			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Orthostatic hypotension			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Chest discomfort			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Drug effect decreased			
subjects affected / exposed	2 / 81 (2.47%)	2 / 78 (2.56%)	
occurrences (all)	2	2	
Face oedema			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 81 (2.47%)	2 / 78 (2.56%)	
occurrences (all)	2	2	
Feeling abnormal			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Gait disturbance			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Malaise			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Medical device site irritation			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	8 / 81 (9.88%)	2 / 78 (2.56%)	
occurrences (all)	8	2	
Therapeutic response delayed			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Therapeutic response shortened			
subjects affected / exposed	8 / 81 (9.88%)	3 / 78 (3.85%)	
occurrences (all)	9	4	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Pulmonary oedema			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Delusion			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Hallucination, visual			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Insomnia			

subjects affected / exposed	1 / 81 (1.23%)	3 / 78 (3.85%)	
occurrences (all)	2	3	
Nightmare			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Sleep attacks			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Sleep disorder			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Blood potassium increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Skin injury			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiac failure chronic			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Coronary artery disease			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Akinesia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Cognitive disorder			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 81 (1.23%)	4 / 78 (5.13%)	
occurrences (all)	1	5	
Dysarthria			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Dyskinesia			
subjects affected / exposed	4 / 81 (4.94%)	4 / 78 (5.13%)	
occurrences (all)	4	4	
Dystonia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences (all)	1	3	
Hypersomnia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Hypokinesia			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Parkinson's disease			
subjects affected / exposed	7 / 81 (8.64%)	8 / 78 (10.26%)	
occurrences (all)	8	8	
Restless legs syndrome			
subjects affected / exposed	0 / 81 (0.00%)	3 / 78 (3.85%)	
occurrences (all)	0	3	
Somnolence			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Spinal cord disorder			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	4 / 81 (4.94%)	1 / 78 (1.28%)	
occurrences (all)	4	1	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Colon adenoma			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences (all)	1	2	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	2	
Ocular hyperaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	2 / 81 (2.47%)	1 / 78 (1.28%)	
occurrences (all)	2	1	
Dry mouth			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Dyspepsia			

subjects affected / exposed	2 / 81 (2.47%)	1 / 78 (1.28%)	
occurrences (all)	2	1	
Gastrointestinal disorder			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Hiatus hernia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Lip swelling			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	4 / 81 (4.94%)	3 / 78 (3.85%)	
occurrences (all)	4	9	
Reactive gastropathy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Salivary hypersecretion			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			

subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences (all)	1	2	
Pigmentation disorder			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Haematuria			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences (all)	1	3	
Leukocyturia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Urinary tract disorder			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Urine odour abnormal			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Back pain			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 81 (1.23%)	3 / 78 (3.85%)	
occurrences (all)	1	3	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences (all)	1	2	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	5 / 81 (6.17%)	4 / 78 (5.13%)	
occurrences (all)	5	4	
Respiratory tract infection viral			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 81 (0.00%) 0	1 / 78 (1.28%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 0 / 81 (0.00%) 0	 1 / 78 (1.28%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2016	Interim analyses included.
08 June 2017	Opicapone added as a prohibited treatment and option for another interim analysis added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported