Clinical trial results:
SAFETY AND PHARMACOKINETICS OF ODM-204 IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (CRPC): OPEN, NONRANDOMISED, UNCONTROLLED, MULTICENTRE, DOSE ESCALATION, FIRST-IN-MAN STUDY WITH A DOSE EXPANSION

Summary

EudraCT number	2014-003642-26
Trial protocol	FI GB LV
Global end of trial date	21 January 2019

Results information

Result version number	v1 (current)
This version publication date	05 February 2020
First version publication date	05 February 2020

Trial information

Trial identification

Sponsor protocol code	3116001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02344017
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 104261, clinicaltrials@orionpharma.com
Scientific contact	clinicaltrials@orionpharma.com, Orion Corporation, Orion Pharma, +358 104261, 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	21 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 January 2019
Global end of trial reached?	Yes
Global end of trial date	21 January 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate safety and tolerability of ODM-204 including dose limiting toxicities (DLTs) and the maximum tolerated dose (MTD), if possible.
Study included a planned phase II dose expansion component. The recruitment was discontinued after phase I, in September 2016 after 5 dose levels. The discontinuation decision was done due to decreased steady state exposure in human, especially at higher dose levels. The antitumour activity was modest due to decreased exposures.

Protection of trial subjects:

Adequate medical expertise and facilities to handle possible emergency situations were available throughout the study. Study subjects were carefully monitored during the study. The dose escalation for following cohort were decided with a support of the safety monitoring board after a minimum of 3 patients had provided
evaluable dose limiting toxicity -data.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2015
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	United Kingdom: 7
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Latvia: 5
Worldwide total number of subjects	23
EEA total number of subjects	23

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Male patients with histologically or cytologically confirmed adenocarcinoma of prostate were recruited to this study.

Pre-assignment

Screening details:

Confirmed adenocarcinoma of prostate with documented metastatic disease and prostate cancer progression. Males >18 years with informed consent (IC) obtained. Ongoing GnRH therapy, or after bilateral orchiectomy. Eastern Cooperative Oncology Group (ECOG) performance status 0-2 and estimated life expectancy of at least 3 months.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	50 mg b.i.d

Arm description:

50 mg of ODM-204 twice a day

Arm type	Experimental
Investigational medicinal product name	ODM-204
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

50 mg twice daily with food

Arm title	100 mg b.i.d

Arm description:

100 mg of ODM-204 twice a day

Arm type	Experimental
Investigational medicinal product name	ODM-204
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg twice daily with food

Arm title	200 mg b.i.d

Arm description:

200 mg of ODM-204 twice a day

Arm type	Experimental

Investigational medicinal product name	ODM-204
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
200 mg twice daily (3 patients with food, 3 patients fasted)

Arm title	300 mg b.i.d

Arm description:
300 mg of ODM-204 twice a day

Arm type	Experimental
Investigational medicinal product name	ODM-204
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
300 mg twice daily with food

Arm title	500 mg b.i.d

Arm description:
500 mg of ODM-204 twice a day

Arm type	Experimental
Investigational medicinal product name	ODM-204
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
500 mg twice daily with food

Number of subjects in period 1	50 mg b.i.d	100 mg b.i.d	200 mg b.i.d
Started	3	3	6
Completed	3	3	6

Number of subjects in period 1	300 mg b.i.d	500 mg b.i.d
Started	7	4
Completed	7	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	23	23	
Age categorical Units: Subjects			
Adults (18-64 years)	4	4	
From 65-84 years	19	19	
Gender categorical Units: Subjects			
Male	23	23	

End points

End points reporting groups	
Reporting group title	50 mg b.i.d
Reporting group description: 50 mg of ODM-204 twice a day	
Reporting group title	100 mg b.i.d
Reporting group description: 100 mg of ODM-204 twice a day	
Reporting group title	200 mg b.i.d
Reporting group description: 200 mg of ODM-204 twice a day	
Reporting group title	300 mg b.i.d
Reporting group description: 300 mg of ODM-204 twice a day	
Reporting group title	500 mg b.i.d
Reporting group description: 500 mg of ODM-204 twice a day	

Primary: Frequency of adverse events	
End point title	Frequency of adverse events[1]
End point description:	
End point type	Primary
End point timeframe: Treatment emergent adverse events	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics because only part 1 was conducted.

End point values	50 mg b.i.d	100 mg b.i.d	200 mg b.i.d	300 mg b.i.d
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Subjects	3	3	6	7

End point values	500 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Subjects	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment emergent adverse events	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	50 mg b.i.d
Reporting group description:	
50 mg of ODM-204 twice a day	
Reporting group title	200 mg b.i.d
Reporting group description:	
200 mg of ODM-204 twice a day	
Reporting group title	100 mg b.i.d
Reporting group description:	
100 mg of ODM-204 twice a day	
Reporting group title	300 mg b.i.d
Reporting group description:	
300 mg of ODM-204 twice a day	
Reporting group title	500 mg b.i.d
Reporting group description:	
500 mg of ODM-204 twice a day	

Serious adverse events	50 mg b.i.d	200 mg b.i.d	100 mg b.i.d
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (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			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (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

Serious adverse events	300 mg b.i.d	500 mg b.i.d	

Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (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	50 mg b.i.d	200 mg b.i.d	100 mg b.i.d
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Peripheral coldness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	3	1
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Suprapubic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood potassium decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
General physical condition abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lymph node palpable			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysarthria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Diarrhoea			

subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastric haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
Pathological fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tendon pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	300 mg b.i.d	500 mg b.i.d	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Peripheral coldness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	
occurrences (all)	4	0	
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
General physical health deterioration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Infusion site extravasation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pyrexia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Suprapubic pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Thirst			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Depressed mood			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Depression			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Insomnia			

subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Restlessness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood potassium decreased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Blood urine present			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
General physical condition abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Lymph node palpable			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Wrist fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Dysarthria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Restless legs syndrome			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Gastric haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Oesophagitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	2 / 7 (28.57%)	1 / 4 (25.00%)	
occurrences (all)	2	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Groin pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pathological fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Tendon pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	1 / 4 (25.00%)	
occurrences (all)	4	1	
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2014	Max daily dose informed, interruption rule of study treatment, dose escalation stopping criteria and SMB role added.
09 January 2015	Additional inclusion criteria: Experimental treatment was to be assessed only in patients for whom no standard treatment was sufficient.
02 April 2015	Use of Prednison was clarified, the dosing regimen was clarified, and some discrepancies were corrected.
06 November 2015	Additional cohorts were added to investigate whether dosing in the fasted state or with higher dosing frequency (t.i.d.) increases the plasma ODM-204 exposure.
08 March 2016	One dose increase at the time of progression was allowed. Back-up investigational product details added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported