Clinical trial results:
A Study in Japan and Ex-Japan to Characterize the Pharmacokinetic and Pharmacodynamic Response to Orteronel (TAK-700) in Chemotherapy-Naïve Patients With Castration-Resistant Prostate Cancer

Summary

EudraCT number	2012-001539-30
Trial protocol	IE GR GB NL
Global end of trial date	01 September 2016

Results information

Result version number	v1 (current)
This version publication date	06 February 2018
First version publication date	06 February 2018

Trial information

Trial identification

Sponsor protocol code	C21013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01666314
WHO universal trial number (UTN)	U1111-1179-5750

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	One Takeda Parkway, Deerfield, IL, Japan, 60015
Public contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.com
Scientific contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.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	01 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine whether orteronel plus prednisone more effectively reduces serum testosterone levels, compared to placebo plus prednisone when administered to subjects in Japan.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2012
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	Japan: 65
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Ireland: 13
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	137
EEA total number of subjects	39

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)	32
From 65 to 84 years	101
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 43 investigative sites in Japan, United States, Greece, Australia, Netherlands, Ireland and United Kingdom from 20 August 2012 to 01 September 2016.

Pre-assignment

Screening details:

Male participants with a diagnosis of adenocarcinoma of the prostate were enrolled in the study. In Japan, participants were randomized to 200 mg orteronel, Placebo, 300 mg orteronel, or Placebo, BID, in a ratio of 2:1:2:1; ex-Japan participants were randomized to 200 mg orteronel, Placebo, 400 mg orteronel, or Placebo, BID, in a ratio of 2:1:2:1.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Orteronel 200 mg (Japan)

Arm description:

Orteronel placebo-matching tablets or Orteronel 200 mg, tablets, orally, twice daily (BID) in Cycle 1 (28 days) followed by orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily continuously throughout the study.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel placebo-matching 200 mg tablets, orally, twice daily in Cycle 1 (28 days) in Japan for up to 2.5 years.

Investigational medicinal product name	Orteronel
Investigational medicinal product code	TAK-700
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel 200 mg, tablets, orally, twice daily in 28-day cycles in Japan for up to 2.5 years.

Arm title	Placebo + Orteronel 300 mg (Japan)

Arm description:

Orteronel placebo-matching tablets or Orteronel 300 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Arm type	Experimental

Investigational medicinal product name	Orteronel
Investigational medicinal product code	TAK-700
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel 300 mg tablets, orally, twice daily in Cycle 1 in 28-day cycles in Japan for up to 2.5 years.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel placebo-matching 300 mg tablets, orally, twice daily in Cycle 1 in 28-day cycles in Japan for up to 2.5 years.

Arm title	Placebo + Orteronel 200 mg (Ex-Japan)

Arm description:

Orteronel placebo-matching tablets, or Orteronel 200 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 200 mg, tablets, orally, twice daily in 28 day cycles outside of Japan (Ex-Japan) for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Arm type	Experimental
Investigational medicinal product name	Orteronel
Investigational medicinal product code	TAK-700
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel 200 mg tablets, orally, twice daily in 28-day cycles outside of Japan (Ex-Japan) for up to 2.5 years.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel placebo-matching 200 mg tablets, orally, twice daily in Cycle 1 outside of Japan (Ex-Japan) for up to 2.5 years.

Arm title	Placebo + Orteronel 400 mg (Ex-Japan)

Arm description:

Orteronel placebo-matching tablets, or Orteronel 400 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel placebo-matching 400 mg tablets, orally, twice daily in Cycle 1 Ex-Japan for up to 2.5 years.

Investigational medicinal product name	Orteronel
Investigational medicinal product code	TAK-700
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Orteronel 400 mg, tablets, orally, twice daily in 28-day cycles Ex-Japan for up to 2.5.years.

Number of subjects in period 1	Placebo + Orteronel 200 mg (Japan)	Placebo + Orteronel 300 mg (Japan)	Placebo + Orteronel 200 mg (Ex-Japan)
Started	33	32	36
Completed	0	0	0
Not completed	33	32	36
Unsatisfactory Therapeutic Response	7	2	1
Consent withdrawn by subject	1	1	2
Adverse event, non-fatal	3	13	7
Progressive Disease	11	9	19
Symptomatic Deterioration	1	-	2
Reason not Specified	10	7	5

Number of subjects in period 1	Placebo + Orteronel 400 mg (Ex-Japan)
Started	36
Completed	0
Not completed	36
Unsatisfactory Therapeutic Response	1
Consent withdrawn by subject	3
Adverse event, non-fatal	7
Progressive Disease	20
Symptomatic Deterioration	-
Reason not Specified	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	137	137	
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)	32	32	
From 65-84 years	101	101	
85 years and over	4	4	
Age Continuous Units: years			
arithmetic mean	70.6		
full range (min-max)	49 to 88	-	
Gender, Male/Female Units: Subjects			
Female	0	0	
Male	137	137	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	136	136	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
White	70	70	
Black or African American	2	2	
Asian - Japanese	65	65	
Region of Enrollment Units: Subjects			
Japan	65	65	
Australia	8	8	
Greece	10	10	
Ireland	13	13	
Netherlands	13	13	
United Kingdom	3	3	
United States	25	25	

Study Specific Characteristic | Height			
Units: cm			
arithmetic mean	169.29		
full range (min-max)	151.0 to 189.0	-	
Study Specific Characteristic | Weight			
Units: kg			
arithmetic mean	77.77		
full range (min-max)	44.7 to 134.6	-	
Study Specific Characteristic | Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean	26.96		
full range (min-max)	16.7 to 40.3	-	

End points

End points reporting groups

Reporting group title	Placebo + Orteronel 200 mg (Japan)
Reporting group description:	
Orteronel placebo-matching tablets or Orteronel 200 mg, tablets, orally, twice daily (BID) in Cycle 1 (28 days) followed by orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily continuously throughout the study.	
Reporting group title	Placebo + Orteronel 300 mg (Japan)
Reporting group description:	
Orteronel placebo-matching tablets or Orteronel 300 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Reporting group title	Placebo + Orteronel 200 mg (Ex-Japan)
Reporting group description:	
Orteronel placebo-matching tablets, or Orteronel 200 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 200 mg, tablets, orally, twice daily in 28 day cycles outside of Japan (Ex-Japan) for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Reporting group title	Placebo + Orteronel 400 mg (Ex-Japan)
Reporting group description:	
Orteronel placebo-matching tablets, or Orteronel 400 mg, tablets, orally, twice daily in Cycle 1 followed by orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Subject analysis set title	Orteronel 200 mg (Japan)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Subject analysis set title	Orteronel 300 mg (Japan)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Subject analysis set title	Orteronel 200 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Subject analysis set title	Orteronel 400 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	
Subject analysis set title	Placebo (Japan)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Orteronel placebo-matching tablets, orally, twice daily in Cycle 1. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.	

Subject analysis set title	Placebo (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel placebo-matching tablets, orally, twice daily in Cycle 1. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Placebo (Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel placebo-matching tablets, orally, twice daily in Cycle 1 (28 days). Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Placebo (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel placebo-matching tablets, orally, twice daily in Cycle 1. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 400 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 300 mg (Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 400 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 300 mg (Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 400 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Subject analysis set title	Orteronel 200 mg (Japan and ex-Japan)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in Japan and ex-Japan for up to 3 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Primary: Percentage of Participants with Serum Testosterone Levels Reduced to ≤ 2 ng/dL After 4 Weeks of Treatment in Japan

End point title	Percentage of Participants with Serum Testosterone Levels Reduced to ≤ 2 ng/dL After 4 Weeks of Treatment in Japan

End point description:

Serum Ultra-sensitive testosterone was measured by liquid chromatography at a central laboratory.

End point type	Primary

End point timeframe:

Baseline and Week 4

End point values	Orteronel 300 mg (Japan)	Placebo (Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	21		
Units: percentage of participants				
number (confidence interval 95%)	100.0 (84.6 to 100.0)	86.0 (63.7 to 97.0)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo (Japan) v Orteronel 300 mg (Japan)
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1078
Method	Fisher exact

Secondary: Percentage of Participants with Serum Testosterone Levels Reduced to ≤ 2 ng/dL in Ex-Japan

End point title	Percentage of Participants with Serum Testosterone Levels Reduced to ≤ 2 ng/dL in Ex-Japan
End point description:	
Serum Ultra-sensitive testosterone was measured by liquid chromatography at a central laboratory.	
End point type	Secondary
End point timeframe:	
Baseline and Week 4	

End point values	Orteronel 400 mg (Ex-Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	23		
Units: percentage of participants				
number (confidence interval 95%)	79.0 (57.8 to 92.9)	48.0 (26.8 to 69.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (Ex-Japan) v Orteronel 400 mg (Ex-Japan)
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0355
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	4.145

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9895
upper limit	18.7606

Secondary: Percent Change from Baseline in Serum Testosterone Level after 4 Weeks of Treatment

End point title	Percent Change from Baseline in Serum Testosterone Level after 4 Weeks of Treatment

End point description:

Serum Ultra-sensitive testosterone was measured by liquid chromatography at a central laboratory.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	21	22
Units: percent change				
arithmetic mean (standard deviation)	-97.245 (± 1.2548)	-96.812 (± 2.7055)	-86.268 (± 37.2015)	-53.954 (± 118.8050)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	20		
Units: percent change				
arithmetic mean (standard deviation)	-87.666 (± 10.4250)	-63.702 (± 43.3941)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Serum Testosterone Level after 12 Weeks of Treatment

End point title	Percent Change from Baseline in Serum Testosterone Level after 12 Weeks of Treatment

End point description:

Serum Ultra-sensitive testosterone was measured by liquid chromatography at a central laboratory.

End point type	Secondary

End point timeframe:
Baseline and Week 12

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	26	28	31
Units: percent change				
arithmetic mean (standard deviation)	-95.804 (± 5.3367)	-95.703 (± 5.7468)	-91.311 (± 17.5217)	-14.442 (± 406.3116)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Prostate-Specific Antigen Reduction ≥ 50% (PSA50) after 4 Weeks of Treatment

End point title	Percentage of Participants with Prostate-Specific Antigen Reduction ≥ 50% (PSA50) after 4 Weeks of Treatment

End point description:
A 50% PSA response rate (PSA50) was defined as PSA reduction ≥ 50% from Baseline.

End point type	Secondary

End point timeframe:
Baseline and Week 4

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: percentage of participants				
number (confidence interval 95%)	50.0 (28.2 to 71.8)	41.0 (20.7 to 63.6)	48.0 (27.8 to 68.7)	46.0 (25.6 to 67.2)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: percentage of participants				
number (confidence interval 95%)	48.0 (25.7 to 70.2)	17.0 (5.0 to 38.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PSA50 after 12 Weeks of Treatment

End point title	Percentage of Participants with PSA50 after 12 Weeks of Treatment

End point description:

A 50% PSA response rate (PSA50) was defined as PSA reduction ≥ 50% from Baseline.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	32	36	36
Units: percentage of participants				
number (confidence interval 95%)	55.0 (36.4 to 71.9)	47.0 (29.1 to 65.3)	56.0 (38.1 to 72.1)	44.0 (27.9 to 61.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Testosterone

End point title	Absolute Values for Testosterone

End point description:

Serum Ultra-sensitive testosterone was measured by liquid chromatography at a central laboratory.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 8 and Cycle 2 Day 1

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: ng/dL				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	9.079 (± 4.4581)	10.148 (± 4.6504)	9.263 (± 5.6572)	14.588 (± 13.9833)
Cycle 1 Day 8 (n=22, 22, 20, 21, 20, 19)	0.213 (± 0.0449)	0.251 (± 0.1727)	0.345 (± 0.2770)	6.658 (± 20.4347)
Cycle 2 Day 1 (n=22, 22, 21, 22, 21, 20)	0.203 (± 0.0145)	0.270 (± 0.2311)	0.266 (± 0.1837)	11.720 (± 45.1753)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: ng/dL				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	9.749 (± 3.8460)	9.173 (± 5.6123)		
Cycle 1 Day 8 (n=22, 22, 20, 21, 20, 19)	1.957 (± 2.2843)	3.509 (± 4.3471)		
Cycle 2 Day 1 (n=22, 22, 21, 22, 21, 20)	1.096 (± 0.7751)	3.095 (± 3.7254)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Dehydroepiandrosterone Sulfate (DHEA-S)

End point title	Absolute Values for Dehydroepiandrosterone Sulfate (DHEA-S)

End point description:

Serum Ultra low level quantification of DHEA-S was measured by liquid chromatography and mass spectrometry (LC/MS) at a central laboratory.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 8 and Cycle 2 Day 1

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	2529.0 (± 1309.39)	2340.9 (± 1606.36)	1783.0 (± 1554.76)	2155.7 (± 1591.51)
Cycle 1 Day 8 (n=22, 22, 23, 22, 21, 20)	63.4 (± 55.11)	71.8 (± 80.23)	116.9 (± 161.01)	226.6 (± 328.70)
Cycle 2 Day 1 (n=22, 22, 22, 22, 21, 20)	14.5 (± 21.83)	36.3 (± 123.48)	21.5 (± 25.68)	180.6 (± 527.03)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		

Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	1928.0 (± 1306.59)	2601.7 (± 3009.41)		
Cycle 1 Day 8 (n=22, 22, 23, 22, 21, 20)	414.9 (± 392.63)	973.8 (± 1677.95)		
Cycle 2 Day 1 (n=22, 22, 22, 22, 21, 20)	268.9 (± 357.32)	815.7 (± 1918.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Adrenocorticotropic Hormone (ACTH)

End point title	Absolute Values for Adrenocorticotropic Hormone (ACTH)
End point description:	
Serum ACTH was measured by immunometric assay at the central laboratory.	
End point type	Secondary
End point timeframe:	
Baseline, Cycle 1 Day 8 and Cycle 2 Day 1	

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: pmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	5.5 (± 2.54)	8.3 (± 4.98)	6.0 (± 4.05)	6.4 (± 4.04)
Cycle 1 Day 8 (n=22, 22, 21, 18, 21, 22)	2.3 (± 1.55)	3.0 (± 2.70)	3.8 (± 3.04)	3.2 (± 2.56)
Cycle 2 Day 1 (n=22, 22, 24, 22, 21, 22)	1.7 (± 1.08)	2.7 (± 2.17)	3.7 (± 4.38)	3.6 (± 2.26)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: pmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	5.0 (± 1.66)	4.7 (± 2.06)		
Cycle 1 Day 8 (n=22, 22, 21, 18, 21, 22)	3.1 (± 2.68)	3.1 (± 2.62)		
Cycle 2 Day 1 (n=22, 22, 24, 22, 21, 22)	1.7 (± 1.19)	3.0 (± 1.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Corticosterone

End point title	Absolute Values for Corticosterone

End point description:

Serum Corticosterone was measured by high pressure liquid chromatography with mass spectrometry at the central laboratory.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 8 and Cycle 2 Day 1

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	6.515 (± 4.8246)	7.768 (± 6.8625)	10.030 (± 7.7341)	17.975 (± 35.0695)
Cycle 1 Day 8 (n=22, 22, 23, 21, 21, 20)	11.067 (± 14.4220)	9.709 (± 13.4538)	48.668 (± 66.3904)	60.301 (± 77.5434)
Cycle 2 Day 1 (n=22, 22, 23, 22, 21, 20)	11.108 (± 9.0708)	14.654 (± 9.2064)	29.929 (± 35.5565)	47.204 (± 53.4566)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	5.946 (± 3.4433)	6.317 (± 4.1467)		
Cycle 1 Day 8 (n=22, 22, 23, 21, 21, 20)	1.530 (± 1.6404)	5.598 (± 7.1366)		
Cycle 2 Day 1 (n=22, 22, 23, 22, 21, 20)	0.758 (± 0.5108)	4.321 (± 6.4063)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Cortisol

End point title	Absolute Values for Cortisol

End point description:

Serum Cortisol was measured by immunometric assay at the central laboratory.

End point type	Secondary

End point timeframe:

Baseline, Cycle 1 Day 8 and Cycle 2 Day 1

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	371.3 (± 119.38)	383.4 (± 125.98)	449.0 (± 131.54)	446.8 (± 193.09)
Cycle 1 Day 8 (n=22, 22, 24, 22, 21, 23)	49.5 (± 25.53)	55.5 (± 55.97)	100.9 (± 87.38)	122.0 (± 88.70)
Cycle 2 Day 1 (n=22, 22, 24, 23, 20, 21)	49.2 (± 21.71)	54.3 (± 39.93)	97.2 (± 85.66)	109.1 (± 83.19)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: nmol/L				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	366.5 (± 116.69)	384.8 (± 117.14)		
Cycle 1 Day 8 (n=22, 22, 24, 22, 21, 23)	82.3 (± 46.16)	175.8 (± 107.82)		
Cycle 2 Day 1 (n=22, 22, 24, 23, 20, 21)	53.9 (± 24.92)	149.6 (± 122.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values for Prostate-Specific Antigen (PSA)

End point title	Absolute Values for Prostate-Specific Antigen (PSA)

End point description:

Serum PSA was measured at the central laboratory.

End point type	Secondary

End point timeframe:

Baseline and Cycle 2 Day 1

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	27.227 (± 24.8821)	97.504 (± 293.9496)	165.992 (± 368.5016)	100.237 (± 210.5675)
Cycle 2 Day 1 (n=22, 22, 24, 23, 20, 21)	18.005 (± 16.9858)	38.892 (± 95.0124)	117.257 (± 286.1870)	56.437 (± 97.1621)

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (n=22, 22, 25, 24, 21, 23)	37.588 (± 48.9413)	133.238 (± 189.9345)		
Cycle 2 Day 1 (n=22, 22, 24, 23, 20, 21)	24.325 (± 46.9725)	152.940 (± 261.9735)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax: Maximum Observed Plasma Concentration for Orteronel and M-I Metabolite

End point title	Cmax: Maximum Observed Plasma Concentration for Orteronel and M-I Metabolite

End point description:

Maximum observed plasma concentration (Cmax) is the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Orteronel	1520 (± 23.9)	2210 (± 33.9)	1300 (± 59.7)	1610 (± 50.3)
Orteronel Metabolite M-I	272 (± 33.1)	422 (± 37.0)	199 (± 61.9)	261 (± 47.2)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-12): Area Under the Plasma Concentration-Time Curve From Time 0 to 12 Hours Post-dose for Orteronel and M-I Metabolite

End point title	AUC(0-12): Area Under the Plasma Concentration-Time Curve From Time 0 to 12 Hours Post-dose for Orteronel and M-I Metabolite

End point description:

AUC(0-12) is measure of area under the curve over the dosing interval where the length of the dosing interval is time 0 to 12 hours in this study.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Orteronel	8810 (± 16.4)	12800 (± 31.2)	7830 (± 51.1)	10200 (± 41.4)
Orteronel Metabolite M-I	2130 (± 28.3)	3290 (± 33.8)	1570 (± 65.5)	2080 (± 44.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Orteronel and M-I Metabolite

End point title	Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Orteronel and M-I Metabolite

End point description:

Tmax: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: hours				
median (full range (min-max))				
Orteronel	2.97 (1.00 to 5.10)	2.43 (1.00 to 4.97)	2.00 (0.500 to 7.93)	1.92 (0.500 to 5.00)
Orteronel Metabolite M-I	5.00 (2.03 to 8.10)	4.98 (2.00 to 8.23)	5.05 (1.03 to 11.1)	4.98 (1.22 to 11.2)

Statistical analyses

No statistical analyses for this end point

Secondary: AE (0-24) Cumulative Amount of Drug Excreted into the Urine for Orteronel and MI-Metabolite

End point title	AE (0-24) Cumulative Amount of Drug Excreted into the Urine for Orteronel and MI-Metabolite

End point description:

Cumulative amount of urine excreted time 0 to 24 hour.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: mg				
geometric mean (geometric coefficient of variation)				
Orteronel	115.0 (± 26.0)	164.0 (± 26.2)	95.3 (± 31.9)	161.0 (± 41.4)
Orteronel Metabolite M-I	39.6 (± 31.5)	62.5 (± 26.6)	30.0 (± 40.1)	52.8 (± 46.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax,ss: Maximum Observed Plasma Concentration at Steady State for

Orteronel and MI-Metabolite	
End point title	Cmax,ss: Maximum Observed Plasma Concentration at Steady State for Orteronel and MI-Metabolite
End point description:	
Maximum observed steady-state plasma concentration during a dosing interval.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 8 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose	

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Orteronel	2180 (± 22.4)	3210 (± 31.5)	1840 (± 37.1)	3100 (± 45.0)
Orteronel Metabolite M-I	565 (± 32.4)	864 (± 39.5)	485 (± 75.4)	761 (± 81.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax,ss: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax at Steady State for Orteronel and M-I Metabolite	
End point title	Tmax,ss: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax at Steady State for Orteronel and M-I Metabolite
End point description:	
Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax at steady state.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 8 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose	

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: hours				
median (confidence interval 95%)				
Orteronel	2.05 (1.00 to 5.08)	2.96 (1.00 to 5.17)	2.00 (0.550 to 5.17)	1.98 (0.500 to 3.08)
Orteronel Metabolite M-I	3.08 (2.00 to 5.17)	4.78 (2.00 to 8.13)	3.00 (1.00 to 5.07)	3.00 (0 to 8.00)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-tau): Area Under the Plasma Concentration-time Curve from Time 0 to Time tau Over the Dosing Interval for Orteronel and M-I Metabolite

End point title	AUC(0-tau): Area Under the Plasma Concentration-time Curve from Time 0 to Time tau Over the Dosing Interval for Orteronel and M-I Metabolite

End point description:

Area under the plasma concentration-time curve during a dosing interval, where tau is the length of the dosing interval.

End point type	Secondary

End point timeframe:

Cycle 1 Day 8 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Orteronel	13300 (± 20.4)	20400 (± 36.1)	12600 (± 36.2)	20000 (± 55.0)
Orteronel Metabolite M-I	4840 (± 35.0)	7460 (± 46.3)	4340 (± 69.4)	6590 (± 78.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Rac: Accumulation index for Orteronel and M-I metabolite

End point title	Rac: Accumulation index for Orteronel and M-I metabolite

End point description:

Rac was calculated as the ratio of AUCtau to AUC12hr.

End point type	Secondary

End point timeframe:

Cycle 1 Day 8 Predose, 0.5, 1, 2, 3, 5, 8, 12 hours post-dose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	25	24
Units: ratio				
geometric mean (geometric coefficient of variation)				
Orteronel	1.51 (± 9.1)	1.59 (± 46.6)	1.62 (± 39.3)	1.97 (± 90.5)
Orteronel Metabolite M-I	2.27 (± 17.5)	2.26 (± 43.0)	2.76 (± 45.0)	3.17 (± 77.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough,ss: Observed Predose Plasma Concentration at Steady State for Orteronel and M-I Metabolite

End point title	Ctrough,ss: Observed Predose Plasma Concentration at Steady State for Orteronel and M-I Metabolite

End point description:

Observed predose plasma concentration at steady state.

End point type	Secondary

End point timeframe:

Cycle 1 Day 8 Predose

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	22	24	22
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Orteronel	710 (± 28.1)	1060 (± 63.7)	807 (± 45.4)	899 (± 59.8)
Orteronel Metbolite M-I	291 (± 47.1)	444 (± 66.7)	314 (± 68.6)	417 (± 58.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Treatment-Emergent Adverse events (AEs) and Serious Adverse Events (SAEs)

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (eg, a clinically significant abnormal laboratory finding),symptom, or disease temporally associated with the use of a drug, whether

or not it is considered related to the drug. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study A serious adverse event is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant.

End point type	Secondary

End point timeframe:

From signing of the informed consent form through 30 days after the last dose of study drug, approximately 3.2 years

End point values	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)	Orteronel 200 mg (Ex-Japan)	Orteronel 400 mg (Ex-Japan)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	32	36	36
Units: participants				
AE	33	32	36	36
SAE	8	18	16	12

End point values	Placebo (Japan)	Placebo (Ex-Japan)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	23		
Units: participants				
AE	7	18		
SAE	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From signing of the informed consent form through 30 days after the last dose of study drug, approximately 3.2 years for serious adverse events and up to data-cut-off 12-Sep-2013 for non-serious adverse events.

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment. Adverse events were summarized as per the treatment received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Orteronel placebo-matching tablets, orally, twice daily in Cycle 1 (28 days). Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Reporting group title	Orteronel 200 mg (Japan)

Reporting group description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Reporting group title	Orteronel 300 mg (Japan)

Reporting group description:

Orteronel 300 mg, tablets, orally, twice daily in 28 day cycles in Japan for up to 2.8 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Reporting group title	Orteronel 200 mg (Ex-Japan)

Reporting group description:

Orteronel 200 mg, tablets, orally, twice daily in 28 day cycles in for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Reporting group title	Orteronel 400mg (Ex-Japan)

Reporting group description:

Orteronel 400 mg, tablets, orally, twice daily in 28 day cycles Ex-Japan for up to 3.1 years. Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg twice daily (BID) continuously throughout the study.

Serious adverse events	Placebo	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 44 (22.73%)	8 / 33 (24.24%)	18 / 32 (56.25%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Lung adenocarcinoma			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Cancer pain			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Rectal cancer			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Renal neoplasm			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Gastric cancer			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Neoplasm Malignant			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic Carcinoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Metastatic Pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Venous thrombosis limb			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Hypertension			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Orthostatic Hypotension			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Asthenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Fatigue			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Device occlusion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Pleural effusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Investigations			
Pancreatic enzymes increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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			
Head injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Lumbar Vertebral Fracture			

subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Thoracic Vertebral Fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
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 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Coronary Artery Stenosis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Myocardial Ischaemia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Cardiac arrest			

subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Balance disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Aphasia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Spinal cord compression			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Altered State Of Consciousness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Parkinson's disease			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 44 (2.27%)	1 / 33 (3.03%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 44 (2.27%)	1 / 33 (3.03%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Constipation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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 haemorrhage			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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

Large Intestine Polyp			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Vomitting			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Gastrointestinal Angiodysplasia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Bile Duct Stone			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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			

Dermatitis exfoliative			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Urinary tract obstruction			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Acute Kidney Injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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 Colic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Musculoskeletal and connective tissue disorders			
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Ligament Ossification			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pathological Fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Arthralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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			
Pneumonia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Escherichia sepsis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Respiratory tract infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (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
Septic shock			

subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Urinary tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Sepsis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	0 / 32 (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
Pyelonephritis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (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

Serious adverse events	Orteronel 200 mg (Ex-Japan)	Orteronel 400mg (Ex-Japan)	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 36 (44.44%)	12 / 36 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung Neoplasm Malignant			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic Carcinoma			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic Pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Hypotension			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthenia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Pancreatic enzymes increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic Vertebral Fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Bones Fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Ischaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (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			
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered State Of Consciousness			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Duodenal ulcer			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (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 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomitting			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Angiodysplasia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Hepatic function abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile Duct Stone			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Kidney Injury			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Colic			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Ligament Ossification			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological Fracture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis viral			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Infection			

subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Orteronel 200 mg (Japan)	Orteronel 300 mg (Japan)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	33 / 33 (100.00%)	32 / 32 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 44 (4.55%)	1 / 33 (3.03%)	3 / 32 (9.38%)
occurrences (all)	2	1	4
Metastatic pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Hot flush			
subjects affected / exposed	7 / 44 (15.91%)	3 / 33 (9.09%)	5 / 32 (15.63%)
occurrences (all)	7	3	5
Hypertension			
subjects affected / exposed	4 / 44 (9.09%)	3 / 33 (9.09%)	3 / 32 (9.38%)
occurrences (all)	4	3	3
Deep vein thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 44 (18.18%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	9	0	3
Oedema peripheral			
subjects affected / exposed	4 / 44 (9.09%)	8 / 33 (24.24%)	6 / 32 (18.75%)
occurrences (all)	4	10	7
Malaise			
subjects affected / exposed	4 / 44 (9.09%)	4 / 33 (12.12%)	6 / 32 (18.75%)
occurrences (all)	5	5	7
Face Oedema			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	2 / 32 (6.25%)
occurrences (all)	0	2	3
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Peripheral swelling			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Seasonal allergy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 33 (6.06%)	2 / 32 (6.25%)
occurrences (all)	2	2	2
Depression			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Investigations			
Lipase increased			
subjects affected / exposed	19 / 44 (43.18%)	25 / 33 (75.76%)	19 / 32 (59.38%)
occurrences (all)	36	46	32
Amylase increased			
subjects affected / exposed	16 / 44 (36.36%)	21 / 33 (63.64%)	19 / 32 (59.38%)
occurrences (all)	21	35	27

Alanine aminotransferase increased			
subjects affected / exposed	6 / 44 (13.64%)	7 / 33 (21.21%)	7 / 32 (21.88%)
occurrences (all)	7	7	11
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 44 (13.64%)	7 / 33 (21.21%)	7 / 32 (21.88%)
occurrences (all)	8	7	11
Gamma-glutamyltransferase increased			
subjects affected / exposed	6 / 44 (13.64%)	5 / 33 (15.15%)	8 / 32 (25.00%)
occurrences (all)	6	6	14
Weight decreased			
subjects affected / exposed	5 / 44 (11.36%)	2 / 33 (6.06%)	6 / 32 (18.75%)
occurrences (all)	5	2	9
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 44 (11.36%)	8 / 33 (24.24%)	4 / 32 (12.50%)
occurrences (all)	5	8	4
Blood creatinine increased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 33 (0.00%)	5 / 32 (15.63%)
occurrences (all)	2	0	5
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 44 (2.27%)	1 / 33 (3.03%)	6 / 32 (18.75%)
occurrences (all)	1	1	7
Blood urea increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	4 / 32 (12.50%)
occurrences (all)	2	0	8
White blood cell count decreased			
subjects affected / exposed	3 / 44 (6.82%)	3 / 33 (9.09%)	3 / 32 (9.38%)
occurrences (all)	5	4	5
Weight increased			
subjects affected / exposed	0 / 44 (0.00%)	4 / 33 (12.12%)	0 / 32 (0.00%)
occurrences (all)	0	4	0
Neutrophil count decreased			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	4	0
Glycosylated haemoglobin increased			

subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
White blood cell count increased			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 44 (4.55%)	3 / 33 (9.09%)	5 / 32 (15.63%)
occurrences (all)	2	4	8
Contusion			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	3 / 32 (9.38%)
occurrences (all)	0	1	3
Rib fracture			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Spinal compression fracture			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	4	0
Skin abrasion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Thoracic vertebral fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Meniscus injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	2 / 44 (4.55%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	2	1	2
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	3 / 44 (6.82%)	2 / 33 (6.06%)	4 / 32 (12.50%)
occurrences (all)	3	2	4
Dizziness			
subjects affected / exposed	1 / 44 (2.27%)	2 / 33 (6.06%)	4 / 32 (12.50%)
occurrences (all)	1	2	5
Hypoaesthesia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	4
Somnolence			
subjects affected / exposed	0 / 44 (0.00%)	5 / 33 (15.15%)	0 / 32 (0.00%)
occurrences (all)	0	6	0
Headache			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Paraesthesia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Increased tendency to bruise			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	1 / 32 (3.13%)
occurrences (all)	0	3	1
Lacrimation increased			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Glaucoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	7 / 44 (15.91%)	8 / 33 (24.24%)	10 / 32 (31.25%)
occurrences (all)	7	9	12
Diarrhoea			
subjects affected / exposed	11 / 44 (25.00%)	4 / 33 (12.12%)	5 / 32 (15.63%)
occurrences (all)	12	4	6
Nausea			
subjects affected / exposed	7 / 44 (15.91%)	5 / 33 (15.15%)	7 / 32 (21.88%)
occurrences (all)	12	6	10
Vomiting			
subjects affected / exposed	3 / 44 (6.82%)	4 / 33 (12.12%)	3 / 32 (9.38%)
occurrences (all)	3	4	11
Abdominal discomfort			
subjects affected / exposed	4 / 44 (9.09%)	4 / 33 (12.12%)	2 / 32 (6.25%)
occurrences (all)	4	4	3
Abdominal pain upper			
subjects affected / exposed	1 / 44 (2.27%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	1	1	3
Abdominal pain			
subjects affected / exposed	2 / 44 (4.55%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	2	2	0
Stomatitis			

subjects affected / exposed	4 / 44 (9.09%)	2 / 33 (6.06%)	2 / 32 (6.25%)
occurrences (all)	4	2	2
Chronic Gastritis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Abdominal distension			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Dental caries			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	3
Pancreatitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	3 / 32 (9.38%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	3 / 44 (6.82%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	3	0	0
Rash maculo-papular			

subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	4	0
Rash erythematous			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	3 / 32 (9.38%)
occurrences (all)	0	1	4
Purpura			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	2 / 32 (6.25%)
occurrences (all)	0	2	2
Dry skin			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Eczema			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Skin atrophy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Rash papular			

subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 44 (2.27%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	1	1	2
Nocturia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	4	0	0
Dysuria			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Pollakiuria			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Renal failure			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	1 / 32 (3.13%)
occurrences (all)	0	3	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	11 / 44 (25.00%)	3 / 33 (9.09%)	8 / 32 (25.00%)
occurrences (all)	16	3	9
Back pain			

subjects affected / exposed	3 / 44 (6.82%)	2 / 33 (6.06%)	3 / 32 (9.38%)
occurrences (all)	3	2	3
Arthralgia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	3	0	0
Muscular weakness			
subjects affected / exposed	2 / 44 (4.55%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	2
Musculoskeletal pain			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 44 (4.55%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	2	0	0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
Osteoporosis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	7 / 44 (15.91%)	8 / 33 (24.24%)	8 / 32 (25.00%)
occurrences (all)	7	10	13
Upper respiratory trat infection			
subjects affected / exposed	4 / 44 (9.09%)	3 / 33 (9.09%)	4 / 32 (12.50%)
occurrences (all)	4	4	5
Bronchitis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	0	1	3
Cystitis			
subjects affected / exposed	0 / 44 (0.00%)	3 / 33 (9.09%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Herpes zoster			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Pharyngitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Oral candidiasis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	5 / 44 (11.36%)	9 / 33 (27.27%)	6 / 32 (18.75%)
occurrences (all)	5	10	8
Decreased appetite			
subjects affected / exposed	5 / 44 (11.36%)	1 / 33 (3.03%)	5 / 32 (15.63%)
occurrences (all)	7	1	8
Hyponatraemia			
subjects affected / exposed	4 / 44 (9.09%)	2 / 33 (6.06%)	2 / 32 (6.25%)
occurrences (all)	4	3	2
Dehydration			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	3 / 44 (6.82%)	1 / 33 (3.03%)	2 / 32 (6.25%)
occurrences (all)	3	1	2
Hypokalaemia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	2	2	0
Hyperkalaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 33 (0.00%)	3 / 32 (9.38%)
occurrences (all)	1	0	4
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Hyperlipidaemia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 33 (6.06%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Hypercholesterolaemia			

subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 33 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Orteronel 200 mg (Ex-Japan)	Orteronel 400mg (Ex-Japan)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 36 (97.22%)	36 / 36 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Metastatic pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Vascular disorders			
Hot flush			
subjects affected / exposed	5 / 36 (13.89%)	10 / 36 (27.78%)	
occurrences (all)	5	10	
Hypertension			
subjects affected / exposed	2 / 36 (5.56%)	8 / 36 (22.22%)	
occurrences (all)	2	8	
Deep vein thrombosis			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Flushing			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 36 (52.78%)	15 / 36 (41.67%)	
occurrences (all)	22	17	

Oedema peripheral			
subjects affected / exposed	7 / 36 (19.44%)	5 / 36 (13.89%)	
occurrences (all)	7	6	
Malaise			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Face Oedema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	5 / 36 (13.89%)	4 / 36 (11.11%)	
occurrences (all)	5	5	
Cough			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Productive cough			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Pulmonary embolism			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 36 (16.67%)	4 / 36 (11.11%)	
occurrences (all)	6	4	

Depression			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Anxiety			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Restlessness			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Investigations			
Lipase increased			
subjects affected / exposed	9 / 36 (25.00%)	7 / 36 (19.44%)	
occurrences (all)	10	9	
Amylase increased			
subjects affected / exposed	4 / 36 (11.11%)	6 / 36 (16.67%)	
occurrences (all)	7	10	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	4	1	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	4	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	
occurrences (all)	2	4	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Blood urea increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
White blood cell count decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 36 (5.56%)	5 / 36 (13.89%)	
occurrences (all)	4	6	
Contusion			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	
occurrences (all)	8	0	
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Spinal compression fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Meniscus injury			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Sinus tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 36 (11.11%)	4 / 36 (11.11%)	
occurrences (all)	4	4	
Dizziness			
subjects affected / exposed	3 / 36 (8.33%)	5 / 36 (13.89%)	
occurrences (all)	3	5	
Hypoaesthesia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Somnolence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	4	2	
Paraesthesia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	
occurrences (all)	3	3	
Syncope			

subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	3	
Neuropathy peripheral			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Increased tendency to bruise			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Thrombocytopenia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Lacrimation increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Glaucoma			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 36 (27.78%)	12 / 36 (33.33%)	
occurrences (all)	13	13	
Diarrhoea			
subjects affected / exposed	15 / 36 (41.67%)	13 / 36 (36.11%)	
occurrences (all)	30	16	
Nausea			

subjects affected / exposed	13 / 36 (36.11%)	12 / 36 (33.33%)	
occurrences (all)	17	16	
Vomiting			
subjects affected / exposed	9 / 36 (25.00%)	3 / 36 (8.33%)	
occurrences (all)	12	3	
Abdominal discomfort			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	
occurrences (all)	1	4	
Abdominal pain			
subjects affected / exposed	4 / 36 (11.11%)	3 / 36 (8.33%)	
occurrences (all)	4	3	
Stomatitis			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	
occurrences (all)	4	7	
Chronic Gastritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	1 / 36 (2.78%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Abdominal distension			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dental caries			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pancreatitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Mouth ulceration			

subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	4	
Dysphagia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	3	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	3 / 36 (8.33%)	4 / 36 (11.11%)	
occurrences (all)	4	4	
Rash maculo-papular			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Rash erythematous			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Purpura			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Eczema			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Skin atrophy			

subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	3	2	
Ecchymosis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Hyperhidrosis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Rash pruritic			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Decubitus ulcer			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	3	
Rash papular			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	3	
Dermatitis acneiform			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Nocturia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Dysuria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	1 / 36 (2.78%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Renal failure			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	

Hydronephrosis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Urinary retention			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	8 / 36 (22.22%)	12 / 36 (33.33%)	
occurrences (all)	11	22	
Back pain			
subjects affected / exposed	5 / 36 (13.89%)	3 / 36 (8.33%)	
occurrences (all)	6	3	
Arthralgia			
subjects affected / exposed	5 / 36 (13.89%)	4 / 36 (11.11%)	
occurrences (all)	6	5	
Muscular weakness			
subjects affected / exposed	4 / 36 (11.11%)	4 / 36 (11.11%)	
occurrences (all)	4	4	
Musculoskeletal pain			
subjects affected / exposed	3 / 36 (8.33%)	3 / 36 (8.33%)	
occurrences (all)	4	4	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	
occurrences (all)	4	3	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Osteoporosis			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Musculoskeletal discomfort			

subjects affected / exposed	3 / 36 (8.33%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Myalgia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	4	1	
Bone pain			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Groin pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Upper respiratory trat infection			
subjects affected / exposed	6 / 36 (16.67%)	2 / 36 (5.56%)	
occurrences (all)	7	2	
Bronchitis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	5	3	
Cystitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Herpes zoster			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	

Pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	3 / 36 (8.33%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	4 / 36 (11.11%)	
occurrences (all)	0	6	
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Tooth abscess			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	
occurrences (all)	1	4	
Decreased appetite			
subjects affected / exposed	9 / 36 (25.00%)	7 / 36 (19.44%)	
occurrences (all)	10	8	
Hyponatraemia			
subjects affected / exposed	1 / 36 (2.78%)	4 / 36 (11.11%)	
occurrences (all)	1	4	
Dehydration			
subjects affected / exposed	3 / 36 (8.33%)	4 / 36 (11.11%)	
occurrences (all)	3	5	
Hyperglycaemia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Hypokalaemia			

subjects affected / exposed	5 / 36 (13.89%)	1 / 36 (2.78%)	
occurrences (all)	6	1	
Hyperkalaemia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	4	2	
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 36 (5.56%)	4 / 36 (11.11%)	
occurrences (all)	2	5	
Hypoglycaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Hyperlipidaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Hypomagnesaemia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	2	1	

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