Clinical trial results:
Knee joint replacement over 5 years in patients with knee osteoarthritis. A long term follow up study in patients of the CL3-12911-018 study.

Summary

EudraCT number	2011-004046-18
Trial protocol	CZ DE AT BE PL ES IT DK LT PT
Global end of trial date	30 June 2014

Results information

Result version number	v1 (current)
This version publication date	06 July 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	CL3-12911-040

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284
Public contact	Therapeutic Innovation pole, Institut de Recherches Internationales Servier , 0033 0155724366, clinicaltrials@servier.com
Scientific contact	Therapeutic Innovation pole, Institut de Recherches Internationales Servier , 0033 0155724366, clinicaltrials@servier.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	30 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2014
Global end of trial reached?	Yes
Global end of trial date	30 June 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To collect data on knee joint replacement procedures or procedures practiced in the knee (arthroscopy, osteotomy or other) over 5 years in patients with knee osteoarthritis having participated in the CL3-12911-018 study and having received at least one year (365 days) of CL3-12911-018 study treatment (Strontium Ranelate 1g/2g or placebo).

Protection of trial subjects:

A patient could be prematurely and definitively discontinued from the study for medical (i.e. any new medical condition that may prevent the patient's study participation) or or non-medical reason (including participant's consent withdrawal) or patient lost to follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 71
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Spain: 96
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Belgium: 69
Country: Number of subjects enrolled	Czech Republic: 23
Country: Number of subjects enrolled	Denmark: 151
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Italy: 68
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Canada: 149
Country: Number of subjects enrolled	Estonia: 26
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Romania: 7

Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	United Kingdom: 47
Worldwide total number of subjects	878
EEA total number of subjects	669

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)	303
From 65 to 84 years	569
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

In all, 75 centres in 18 countries from the CL3-12911-018 study (having received at least one year of study treatment) included 878 patients.

Pre-assignment

Screening details:

Of the 1206 patients included in the CL3-12911-018 study with at least one year of study treatment, 878 patients were included in the present study: 288 patients in the former SrRan 1 g group, 296 patients in the former SrRan 2 g group, and 294 patients in the former placebo group.

Period 1

Period 1 title	Whole study period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Former SrRan 1 g

Arm description:

Patients received at least one year (365 days) of treatment of strontium ranelate 1 g during the CL3-12911-018 study, i.e. called in the present study former SrRan 1 g.

Arm type	Experimental
Investigational medicinal product name	Strontium ranelate 1g
Investigational medicinal product code	S12911
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

One sachet of granules containing 1g of strontium ranelate had to be taken daily in the evening at bedtime preferably 2 hours after eating. The content of the sachet was to be mixed with at least 50 mL of tap water (approximately third of a glass) and the suspension obtained should be taken immediately. The sachet should not be taken with meals, calcium or drinks containing milk or calcium.

Arm title	Former SrRan 2 g

Arm description:

Patients received at least one year (365 days) of treatment of strontium ranelate 2 g during the CL3-12911-018 study, i.e. called in the present study former SrRan 2 g.

Arm type	Experimental
Investigational medicinal product name	Strontium ranelate 2g
Investigational medicinal product code	S12911
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

One sachet of granules containing 2g of strontium ranelate had to be taken daily in the evening at bedtime preferably 2 hours after eating. The content of the sachet was to be mixed with at least 50 mL of tap water (approximately third of a glass) and the suspension obtained should be taken immediately. The sachet should not be taken with meals, calcium or drinks containing milk or calcium.

Arm title	Former Placebo

Arm description:

Patients received at least one year (365 days) of Placebo during the CL3-12911-018 study, i.e. called in the present study former Placebo.

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

Dosage and administration details:

One sachet of granules containing placebo had to be taken daily in the evening at bedtime preferably 2 hours after eating. The content of the sachet was to be mixed with at least 50 mL of tap water (approximately third of a glass) and the suspension obtained should be taken immediately. The sachet should not be taken with meals, calcium or drinks containing milk or calcium.

Number of subjects in period 1	Former SrRan 1 g	Former SrRan 2 g	Former Placebo
Started	288	296	294
Completed	6	5	5
Not completed	282	291	289
Study termination	269	281	273
Medical reason	5	1	3
Lost to follow-up	8	9	10
Non-medical reason	-	-	3

Baseline characteristics

Reporting groups

Reporting group title	Whole study period

Reporting group description: -

Reporting group values	Whole study period	Total	
Number of subjects	878	878	
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)	303	303	
From 65-84 years	569	569	
85 years and over	6	6	
Gender categorical Units: Subjects			
Female	618	618	
Male	260	260	

Subject analysis sets

Subject analysis set title	Included Set follow-up
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised patients in the CL3-12911-018 study who are included in the follow-up study.

Reporting group values	Included Set follow-up		
Number of subjects	878		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	303		
From 65-84 years	569		
85 years and over	6		

Gender categorical Units: Subjects			
Female	618		
Male	260		

End points

End points reporting groups

Reporting group title	Former SrRan 1 g

Reporting group description:

Patients received at least one year (365 days) of treatment of strontium ranelate 1 g during the CL3-12911-018 study, i.e. called in the present study former SrRan 1 g.

Reporting group title	Former SrRan 2 g

Reporting group description:

Patients received at least one year (365 days) of treatment of strontium ranelate 2 g during the CL3-12911-018 study, i.e. called in the present study former SrRan 2 g.

Reporting group title	Former Placebo

Reporting group description:

Patients received at least one year (365 days) of Placebo during the CL3-12911-018 study, i.e. called in the present study former Placebo.

Subject analysis set title	Included Set follow-up
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised patients in the CL3-12911-018 study who are included in the follow-up study.

Primary: Knee joint replacement and other knee surgery/procedure

End point title	Knee joint replacement and other knee surgery/procedure[1]

End point description:

End point type	Primary

End point timeframe:

The evaluation criterion was the number of patients who underwent a knee joint replacement defined as a surgery for total prosthesis and/or partial prosthesis.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The study has been prematurely stopped due to strategic reasons, therefore changes have been decided in the statistical analysis : descriptive statistics (quantitative, qualitative) were provided by treatment group depending on the nature of the criteria.

End point values	Former SrRan 1 g	Former SrRan 2 g	Former Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288[2]	296[3]	294[4]	
Units: Number of patient	26	32	27	

Notes:

[2] - Included Set follow-up

[3] - Included Set follow-up

[4] - Included Set follow-up

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

As no medicinal investigational product was delivered and no study specific procedure was planned, no adverse event was expected to be collected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Former SrRan 1 g

Reporting group description:

As no medicinal investigational product was delivered and no study specific procedure was planned, no adverse event was expected to be collected.

Reporting group title	Former SrRan 2 g

Reporting group description:

As no medicinal investigational product was delivered and no study specific procedure was planned, no adverse event was expected to be collected.

Reporting group title	Former Placebo

Reporting group description:

As no medicinal investigational product was delivered and no study specific procedure was planned, no adverse event was expected to be collected.

Serious adverse events	Former SrRan 1 g	Former SrRan 2 g	Former Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 288 (0.00%)	0 / 296 (0.00%)	0 / 294 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Former SrRan 1 g	Former SrRan 2 g	Former Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 288 (0.00%)	0 / 296 (0.00%)	0 / 294 (0.00%)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: As no medicinal investigational product was delivered and no study specific procedure was planned, no adverse event was expected to be collected.

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? Yes

Date	Interruption	Restart date
19 March 2014	The study was prematurely discontinued by the sponsor in relation with strategic reasons. The follow-up of the study lasted at maximum 24 months.	-

Notes:

Limitations and caveats

None reported