Clinical trial results:
A Two-stage 6-month, Multicentre, Randomised, Double-blind, Controlled Study on the Safety and Efficacy of a Single Intra-articular Administration of JTA-004 in Patients with Symptomatic Knee Osteoarthritis

Summary

EudraCT number	2015-002117-30
Trial protocol	BE
Global end of trial date	27 April 2018

Results information

Result version number	v2 (current)
This version publication date	27 November 2019
First version publication date	01 November 2019
Version creation reason	• Changes to summary attachments error in the upload of the summary
Summary attachment (see zip file)	summary report (BT_JTA-KOA1_CSR summary_EudraCT.pdf)

Trial information

Trial identification

Sponsor protocol code	000010/BT

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bone Therapeutics S.A.
Sponsor organisation address	rue Auguste Picard 37, Gosselies, Belgium, B-6041
Public contact	Clinical Trial Information, Bone Therapeutics S.A., jta.koa1@bonetherapeutics.com
Scientific contact	Clinical Trial Information, Bone Therapeutics S.A., jta.koa1@bonetherapeutics.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	07 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2018
Global end of trial reached?	Yes
Global end of trial date	27 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to assess the safety and efficacy of JTA-004® single intra-articular administration in patients suffering from symptomatic osteoarthritis of the knee at the end of the study period (at Month 6).

Safety:
At each follow-up visit, patients will be assessed for the occurrence of any (serious) adverse events using patient open non-directive questionnaire, physical examination (including vital signs), and laboratory measurements. The safety analyses will be based on incidence evaluation of treatment emergent adverse events by preferred term and body system. Laboratory measurements will be compared to the normal laboratory ranges and to laboratory measurements obtained at Baseline Visit.

Efficacy:
Primary study objectives are (i) the selection of the best JTA-004® strength and (ii) the superiority assessment of the best JTA-004® strength efficacy to the reference or (iii) stop the trial at interim analysis for futility.

Protection of trial subjects:

Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 164
Worldwide total number of subjects	164
EEA total number of subjects	164

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)	55
From 65 to 84 years	109
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Men and women, aged 50 to 79 years old, diagnosed with primary knee OA having a previous insufficient/failed response to analgesics and/or nonsteroidal antiinflammatory drugs (NSAIDs).

Period 1

Period 1 title	Screening
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

The Investigators were blind to treatment assignments with respect to the patient evaluation. They recruited, included and assessed patients during the whole study followup period, but did not treat the patients. Investigators were therefore not aware of treatment assignment.
Patients were blind to treatment assignment

Arms

Are arms mutually exclusive?	Yes
Arm title	JTA-004 50 2 mL

Arm description:

Sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg; 2 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 50
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	JTA-004 50 4 mL

Arm description:

sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg/ml. 4 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 50
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	JTA-004 100 2 mL

Arm description:

sodium hyaluronate content was 20 mg and the concentration of clonidine was 100 µg/ml. 2 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 100
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	Synvisc One

Arm description:

Synvisc-One

Arm type	Active comparator
Investigational medicinal product name	Synvisc-One
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intraarticular use

Dosage and administration details:

Single injection

Number of subjects in period 1	JTA-004 50 2 mL	JTA-004 50 4 mL	JTA-004 100 2 mL
Started	41	41	41
Completed	41	41	41

Number of subjects in period 1	Synvisc One
Started	41
Completed	41

Period 2

Period 2 title	Final analysis
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

The Investigators were blind to treatment assignments with respect to the patient evaluation. They recruited, included and assessed patients during the whole study followup period, but did not treat the patients. Investigators were therefore not aware of treatment assignment.
Patients were blind to treatment assignment
same intra-articular injection (performed by the Independent Physicians). As the appearance of the resuspended JTA-004 was differ

Arms

Are arms mutually exclusive?	Yes
Arm title	JTA-004 50 2 mL

Arm description:

Sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg; 2 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 50
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	JTA-004 50 4 mL

Arm description:

sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg/ml. 4 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 50
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	JTA-004 100 2 mL

Arm description:

sodium hyaluronate content was 20 mg and the concentration of clonidine was 100 µg/ml. 2 mL injected

Arm type	Experimental
Investigational medicinal product name	JTA-004 100
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intraarticular use

Dosage and administration details:

Single intra-articular injection

Arm title	Synvisc One

Arm description:

Synvisc-One

Arm type	Active comparator
Investigational medicinal product name	Synvisc-One
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intraarticular use

Dosage and administration details:

Single injection

Number of subjects in period 2	JTA-004 50 2 mL	JTA-004 50 4 mL	JTA-004 100 2 mL
Started	41	41	41
Completed	41	41	41

Number of subjects in period 2	Synvisc One
Started	41
Completed	41

Baseline characteristics

Reporting groups	
Reporting group title	Screening
Reporting group description:	
Adults	

Reporting group values	Screening	Total	
Number of subjects	164	164	
Age categorical			
Adults			
Units: Subjects			
Adults	164	164	
Age continuous			
Age			
Units: years			
arithmetic mean	62.7		
standard deviation	± 7.5	-	
Gender categorical			
Units: Subjects			
Female	112	112	
Male	52	52	

End points

End points reporting groups

Reporting group title	JTA-004 50 2 mL
Reporting group description:	
Sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg; 2 mL injected	
Reporting group title	JTA-004 50 4 mL
Reporting group description:	
sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg/ml. 4 mL injected	
Reporting group title	JTA-004 100 2 mL
Reporting group description:	
sodium hyaluronate content was 20 mg and the concentration of clonidine was 100 µg/ml. 2 mL injected	
Reporting group title	Synvisc One
Reporting group description:	
Synvisc-One	
Reporting group title	JTA-004 50 2 mL
Reporting group description:	
Sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg; 2 mL injected	
Reporting group title	JTA-004 50 4 mL
Reporting group description:	
sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg/ml. 4 mL injected	
Reporting group title	JTA-004 100 2 mL
Reporting group description:	
sodium hyaluronate content was 20 mg and the concentration of clonidine was 100 µg/ml. 2 mL injected	
Reporting group title	Synvisc One
Reporting group description:	
Synvisc-One	

Primary: Womac pain subscale change from baseline

End point title	Womac pain subscale change from baseline
End point description:	
The primary endpoint is the WOMAC® VA3.1 Pain Subscale (subscale A): the individual changes in WOMAC® VA3.1 Pain Subscale Score between Baseline and Month 6 were calculated and compared by analysis of covariance (ANCOVA), adjusted for baseline value, to the Reference group.	
End point type	Primary
End point timeframe:	
Evaluation at month 6	

End point values	JTA-004 100 2 mL	Synvisc One		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: mm				
arithmetic mean (standard deviation)	-26.7 (± 28.9)	-11.3 (± 27.9)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

The primary endpoint is the WOMAC® VA3.1 Pain Subscale (subscale A): the individual changes in WOMAC® VA3.1 Pain Subscale Score between Baseline and Month 6 were calculated and compared by analysis of covariance (ANCOVA), adjusted for baseline value, to the Reference group.

Comparison groups	JTA-004 100 2 mL v Synvisc One
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-9.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.21
upper limit	3.23

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 6 months post injection	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1

Reporting groups	
Reporting group title	JTA-004 50 2 mL
Reporting group description: Sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg; 2 mL injected	
Reporting group title	JTA-004 50 4 mL
Reporting group description: sodium hyaluronate content was 20 mg and the concentration of clonidine was 50 µg/ml. 4 mL injected	
Reporting group title	JTA-004 100 2 mL
Reporting group description: sodium hyaluronate content was 20 mg and the concentration of clonidine was 100 µg/ml. 2 mL injected	
Reporting group title	Synvisc One
Reporting group description: Synvisc-One	

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: non-serious adverse event are discussed in the summary report

Serious adverse events	JTA-004 50 2 mL	JTA-004 50 4 mL	JTA-004 100 2 mL
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 41 (9.76%)	1 / 41 (2.44%)	1 / 41 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Barett's oesophagus			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 41 (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
Diaorrhea			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 41 (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
Hernia eventration			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Rectocele			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 41 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 41 (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
Infections and infestations			
Osteomyelitis acute			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis chronic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 41 (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

Serious adverse events	Synvisc One		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Barett's oesophagus			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diaorrhea			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hernia eventration			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Rectocele			

subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Osteomyelitis acute			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 41		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis chronic			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	JTA-004 50 2 mL	JTA-004 50 4 mL	JTA-004 100 2 mL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)

Non-serious adverse events	Synvisc One		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2016	Amendment 1
10 May 2017	Amendment 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported