Clinical trial results:
Evaluation of the evolution of imaging markers of cartilage degradation in patients with knee osteoarthritis receiving DROGLICAN®: a Pilot Study.

Summary

EudraCT number	2015-005681-37
Trial protocol	BE
Global end of trial date	26 November 2018

Results information

Result version number	v1 (current)
This version publication date	04 November 2021
First version publication date	04 November 2021

Trial information

Trial identification

Sponsor protocol code	CL/BIO/15-005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bioibérica, S.A.U
Sponsor organisation address	Pza Francesc Macià, 7, Barcelona , Spain, 08029
Public contact	Clinical Department , ARTIALIS S.A., investigators_clinicaltrials@artialis.com
Scientific contact	Clinical Department , ARTIALIS S.A., investigators_clinicaltrials@artialis.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	26 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2018
Global end of trial reached?	Yes
Global end of trial date	26 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the evolution of dGEMRIC (delayed Gadolinium-Enhanced Magnetic Resonance Imaging in Cartilage) imaging marker after 6 months of treatment with DROGLICAN®

The second objectives included the use of rescue treatments (Paracetamol, tramadol or oral NSAIDs, excluding COX2 inhibitors) and evaluation of safety and tolerability of the treatment.

Protection of trial subjects:

The clinical trial has been performed according to GCP ICH E6 and the ethical principles that have their origins in the Declaration of Helsinki, last updated in Fortaleza 2013.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	29 June 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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Each patient who signed the informed consent form was considered as screened patient. Patients who signed an informed consent form but were not randomized were considered as screening failures.

Period 1

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

Arms

Arm title	Test product DROGLICAN®
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Chondroitin Sulphate (CS) 200mg / Glucosamine Hydrochloride (GH) 250mg
Investigational medicinal product code	
Other name	DROGLICAN® 200mg/250mg hard-capsules
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

CS = Chondroitin Sulphate; GH = Glucosamine Hydrochloride
Daily dosage of CS 1200 mg and GH 1500 mg during 12 months administrated by taking DROGLICAN® 2 capsules to be taken 3 times a day.

Number of subjects in period 1	Test product DROGLICAN®
Started	22
Completed	10
Not completed	12
Consent withdrawn by subject	6
AE	3
Other	3

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	22	22	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	60.3		
standard deviation	± 10.6	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	4	4	

Subject analysis sets

Subject analysis set title	DROGLICAN®
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients who met the inclusion criteria, received study medication, had a baseline efficacy measurement and at least one corresponding post-baseline efficacy measurement (for the main efficacy variable) and did not present major violations of the protocol. FAS population with dGEMRIC index measured at baseline (T0) and after 6 months treatment (T6).

Reporting group values	DROGLICAN®		
Number of subjects	11		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			

Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	 59.8 ± 10.9		
Gender categorical Units: Subjects			
Female Male	9 2		

End points

End points reporting groups

Reporting group title	Test product DROGLICAN®
Reporting group description: -	
Subject analysis set title	DROGLICAN®
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients who met the inclusion criteria, received study medication, had a baseline efficacy measurement and at least one corresponding post-baseline efficacy measurement (for the main efficacy variable) and did not present major violations of the protocol. FAS population with dGEMRIC index measured at baseline (T0) and after 6 months treatment (T6).

Primary: Change of dGEMRIC index after 6 months of DROGLICAN®

End point title	Change of dGEMRIC index after 6 months of DROGLICAN®[1]

End point description:

Measure of the change of dGEMRIC index (imaging marker) of the cartilage at baseline (T0) and at after 6 months of treatment with DROGLICAN® (T6) for femoral, tibial and patellar cartilage segments (lateral and medial) by Magnetic Resonance Imaging.

dGEMRIC index values remained constants along the 6 months-treatment period and no statistically significant changes were found for any of the compartments.

End point type	Primary

End point timeframe:

From baseline (T0) to 6 months after treatment with DROGLICAN® (T6).

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: Since it was a single-arm study, the statistical analysis performed was descriptive and comparative with respect to baseline. The evolution of dGMERIC index between baseline and 6 months was evaluated using parametric t-test (within treatment differences).

End point values	DROGLICAN®			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: milliseconds				
arithmetic mean (standard deviation)				
T0 - Central femoral condyle lateral	419.9067 (± 120.8584)			
T6 - Central femoral condyle lateral	406.0509 (± 93.3314)			
T0 - Central femoral condyle medial	453.6489 (± 155.2092)			
T6 - Central femoral condyle medial	446.2498 (± 141.5019)			
T0 - Tibia lateral	328.1512 (± 65.6586)			
T6 - Tibia lateral	347.6023 (± 121.0526)			
T0 - Tibia medial	280.653 (± 46.9993)			
T6 - Tibia medial	315.5683 (± 83.1463)			
T0 - Femoral Trochlea lateral	349.5023 (± 64.8379)			
T6 - Femoral Trochlea lateral	340.6526 (± 87.4144)			

T0 - Femoral Trochlea medial	375.1552 (± 118.9147)			
T6 - Femoral Trochlea medial	394.2243 (± 72.6439)			
T0 - Posterior femoral condyle lateral	404.8837 (± 48.6064)			
T6 - Posterior femoral condyle lateral	390.493 (± 46.1298)			
T0 - Posterior femoral condyle medial	403.6964 (± 102.0139)			
T6 - Posterior femoral condyle medial	408.481 (± 119.1598)			
T0 - Patella	402.4983 (± 98.8481)			
T6 - Patella	417.9233 (± 48.5054)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline until the End of the Trial (mean follow up of 375 days for patients exposed to study treatment 12 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Safety population

Reporting group description:

All randomized patients who took at least one dose of the study medication.

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Meningioma malignant			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Multinodular gottery			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 20 (65.00%)		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Lower limb fracture			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Lithiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Constipation			

subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Renal and urinary disorders Lower urinary tract symptoms subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2		
Endocrine disorders Goitre subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain	3 / 20 (15.00%) 3		

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Periarthritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tendon disorder			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2016	Amendment to the protocol to allow the intake of the active treatment to all the patients included in the trial. The amendment responded to investigators remarks about patients' unwillingness to be allocated to the un-treated arm group.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported