Clinical trial results:
PHASE III PROTOCOL COMPARING A MICROFRACTURE TREATMENT TO A CARTIPATCH® CHONDROCYTE GRAFT TREATMENT IN FEMORAL CONDYLE LESIONS

Summary

EudraCT number	2007-003481-18
Trial protocol	BE
Global end of trial date	31 July 2013

Results information

Result version number	v1 (current)
This version publication date	22 July 2021
First version publication date	22 July 2021

Trial information

Trial identification

Sponsor protocol code	CART.III.

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	TBF Genie Tissulaire
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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	16 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2013
Global end of trial reached?	Yes
Global end of trial date	31 July 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Compare the clinical improvement of the IKDC subjective score between the microfracture-treated group and the Cartipatch® chondrocyte graft-treated groups

Protection of trial subjects:

Every cartilage biopsy received was checked to verify their compliance before CARTIPATCH® implantation. Investigators were informed if, for unexpected reasons, the chondrocyte expansion through cell culture could not be initiated. Possible reasons can be either initial poor quality of collected cartilage, or failure during CARTIPATCH® manufacturing. Any adverse event related to cell culture was discussed with the main surgeon and the surgeons in relation with the patient to find a satisfactory solution (performing of a second procurement for instance).

Background therapy: -

Evidence for comparator:

Comparison of CARTIPATCH® to reference therapy (microfracture treatment).

Actual start date of recruitment	11 November 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Israel: 10
Worldwide total number of subjects	32
EEA total number of subjects	19

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

64 patients were expected to be included in the study and to be distributed in two groups of equal size (32 patients per group). As the overall trial enrolment could not be reached in time, inclusion period was delayed several times and study was then early terminated. Finally, a total of 32 patients were included in 6 centers.

Pre-assignment

Screening details:

Forty-six patients were recorded in the study. On this 46 recorded patients, 32 patients were included.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Reference arm : microfracture treatment

Arm type	Reference treatment

No investigational medicinal product assigned in this arm

Arm title	Arm B

Arm description:

Experimental arm, CARTIPATCH®

Arm type	Experimental
Investigational medicinal product name	CARTIPATCH®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Implantation

Dosage and administration details:

Dosage : not applicable
Surgical treatment :
- 1st operative step: Arthroscopy to collect cartilage
- 2nd operative step: Implantation by arthrotomy about 6 weeks following arthroscopy

Number of subjects in period 1	Arm A	Arm B
Started	18	14
Completed	12	9
Not completed	6	5
Graft washed out 1.5 months post-surgery	-	1
Lost to follow-up	2	-
Missing data	1	2

Not treated	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Reference arm : microfracture treatment	
Reporting group title	Arm B
Reporting group description:	
Experimental arm, CARTIPATCH®	

Reporting group values	Arm A	Arm B	Total
Number of subjects	18	14	32
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	14	32
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	33	34	
full range (min-max)	20 to 45	19 to 46	-
Gender categorical			
Units: Subjects			
Female	8	3	11
Male	10	11	21
Lesion size			
Units: cm2			
arithmetic mean	3.46	4.08	
full range (min-max)	2.52 to 5.76	2.50 to 6.25	-

Subject analysis sets	
Subject analysis set title	Treated patients
Subject analysis set type	Per protocol
Subject analysis set description:	
Analysis was done by study arm. All treated patients followed up to 18 months post-surgery were included in the analysis.	

Reporting group values	Treated patients		
Number of subjects	21		

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)	21		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
full range (min-max)			
Gender categorical Units: Subjects			
Female			
Male			
Lesion size Units: cm2			
arithmetic mean			
full range (min-max)			

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Reference arm : microfracture treatment	
Reporting group title	Arm B
Reporting group description:	
Experimental arm, CARTIPATCH®	
Subject analysis set title	Treated patients
Subject analysis set type	Per protocol
Subject analysis set description:	
Analysis was done by study arm. All treated patients followed up to 18 months post-surgery were included in the analysis.	

Primary: Patient part of IKDC subjective score

End point title	Patient part of IKDC subjective score
End point description:	
End point type	Primary
End point timeframe:	
18 months post-surgery	

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: scale from 0 to 100				
arithmetic mean (full range (min-max))	66 (34 to 86)	59 (32 to 98)	63 (32 to 98)	

Statistical analyses

Statistical analysis title	No statistical analysis
Statistical analysis description:	
Statistical analysis to assess difference between treatments was not performed.	
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Not assessed
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Primary: Surgeon part of IKDC score

End point title	Surgeon part of IKDC score

End point description:

End point type	Primary

End point timeframe:

18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: Grade				
Grade A	7	6	13	
Grade B	4	0	4	
Grade C	0	2	2	
Grade D	0	1	1	

Statistical analyses

Statistical analysis title	Surgeon part of IKDC score

Statistical analysis description:

Statistical analysis to assess difference between treatments was not performed.

Comparison groups	Arm A v Arm B
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Not assessed
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Secondary: KOOS clinical scores: SYMPTOMS

End point title	KOOS clinical scores: SYMPTOMS

End point description:

End point type	Secondary

End point timeframe:
18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: 0-100				
arithmetic mean (full range (min-max))	81.6 (53.6 to 92.9)	71.8 (42.9 to 100)	77.4 (42.9 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: KOOS clinical scores: PAIN

End point title	KOOS clinical scores: PAIN

End point description:

End point type	Secondary

End point timeframe:
18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: 0-100				
arithmetic mean (full range (min-max))	78.9 (50.0 to 97.2)	73.5 (47.2 to 100)	76.6 (47.2 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: KOOS clinical scores: ACTIVITY OF DAILY LIVING

End point title	KOOS clinical scores: ACTIVITY OF DAILY LIVING

End point description:

End point type	Secondary

End point timeframe:
18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: 0-100				
arithmetic mean (full range (min-max))	84.6 (63.2 to 100)	77.1 (39.7 to 100)	81.3 (39.7 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: KOOS Clinical scores: SPORTS & RECREATIONAL ACTIVITIES

End point title	KOOS Clinical scores: SPORTS & RECREATIONAL ACTIVITIES

End point description:

End point type	Secondary

End point timeframe:

18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: 0-100				
arithmetic mean (full range (min-max))	56 (0 to 90)	42 (0 to 100)	50 (0 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: KOOS clinical scores: QUALITY OF LIFE

End point title	KOOS clinical scores: QUALITY OF LIFE

End point description:

End point type	Secondary

End point timeframe:

18 months post-surgery

End point values	Arm A	Arm B	Treated patients	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	9	21	
Units: 0-100				
arithmetic mean (full range (min-max))	45.8 (12.5 to 87.5)	52.1 (6.3 to 100)	48.5 (6.3 to 100)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events had to be reported during the whole study period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Arm A (microfracture)

Reporting group description:

No adverse events declared in microfracture group.

Reporting group title	Arm B (CARTIPATCH®)

Reporting group description:

9 adverse events were declared in CARTIPATCH® group affecting 5 patients. 7 of them were probably related to the treatment, 2 were not. 4 of the adverse events were serious adverse events.

Serious adverse events:
- Septic arthritis
- Knee contracture probably due to rehabilitation protocol and chondral defect of medial condyle
- Infection of surgical scar, suspected septic arthritis

Adverse events:
- Fracture of contralateral ankle
- Pain, high blood pressure (not related to CARTIPATCH® graft), tachycardia (not related to CARTIPATCH® graft)
- Knee stiffness in range from 90° to full flexion due to adhesions

Serious adverse events	Arm A (microfracture)	Arm B (CARTIPATCH®)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	3 / 14 (21.43%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Musculoskeletal and connective tissue disorders			
Chondral defect	Additional description: Chondral defect of medial condyle		
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Knee contracture	Additional description: Knee contracture probably due to rehabilitation protocol		
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Septic arthritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site infection	Additional description: Infection of surgical scar with suspected septic arthritis		
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A (microfracture)	Arm B (CARTIPATCH®)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	3 / 14 (21.43%)	
Injury, poisoning and procedural complications			
Fracture of ankle	Additional description: Fracture of contralateral ankle		
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Cardiac disorders			
High blood pressure			
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Knee stiffness	Additional description: Knee stiffness in range from 90° to full flexion due to adhesions		
subjects affected / exposed	0 / 18 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated prematurely because of difficulties in recruiting patients. The decision did not involve any safety reason.
As the statistical analysis of the collected data was not performed, it is impossible to conclude on the product.

Notes: