Clinical trial results:
An Extension Protocol for Participants of Genzyme-Sponsored Prospective, Randomized, Open-Label, Parallel-Group, Multicenter Study of Matrix-Induced Autologous Chondrocyte Implantation (MACI® implant) for the Treatment of Symptomatic Articular Cartilage Defects of the Femoral Condyle Including the Trochlea

Summary

EudraCT number	2009-016970-33
Trial protocol	NL CZ GB SE PL
Global end of trial date	18 March 2015

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	MACI00809

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01251588
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vericel Corporation
Sponsor organisation address	64 Sidney Street, Cambridge, United States, 02139
Public contact	Jon Hopper, Vericel Corporation, 01 (617) 588 5702, jhopper@vcel.com
Scientific contact	Jon Hopper, Vericel Corporation, 01 (617) 588 5702, jhopper@vcel.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	08 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2015
Global end of trial reached?	Yes
Global end of trial date	18 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to examine the 5-year efficacy and safety of Matrix-Induced Autologous Chondrocyte Implantation (MACI® Implant), compared with arthroscopic microfracture, in patients who received study treatment in Genzyme-sponsored study MACI00206 for treatment of symptomatic articular cartilage defects of the femoral condyle, including the trochlea.

Protection of trial subjects:

This is the extension study with no planned intervention. Patients are followed up for long term safety and efficacy, and provided all necessary medical care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2010
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	Netherlands: 58
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	France: 15
Worldwide total number of subjects	128
EEA total number of subjects	128

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)	128
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients who were treated in the parent study (MACI00206) are offered the opportunity to participate in this extension study.

Pre-assignment

Screening details:

128 out of 144 patients who were treated in the parent study (MACI00206) consented to participate in this extension study.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MACI

Arm description:

autologous cultured chondrocytes on porcine collagen membrane implant received in previous MACI00206 study

Arm type	Experimental
Investigational medicinal product name	MACI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Route of administration not applicable

Dosage and administration details:

autologous cultured chondrocytes on porcine collagen membrane: Implantation, received in the parent study (MACI00206)

Arm title	Microfracture

Arm description:

Arthroscopic Microfracture treatment received in the previous MACI00206 study

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	MACI	Microfracture
Started	65	63
Completed	65	63

Period 2	
Period 2 title	Overall
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	MACI

Arm description:

autologous cultured chondrocytes on porcine collagen membrane: Implantation

Arm type	Experimental
Investigational medicinal product name	MACI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Route of administration not applicable

Dosage and administration details:

Autologous cultured chondrocytes on porcine collagen membrane, received study treatment (MACI) in the parent study (MACI00206).

Arm title	Microfracture

Arm description:

Microfracture: Arthroscopic Microfracture received in the parent study (MACI00206)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	MACI	Microfracture
Started	65	63
Completed	65	59
Not completed	0	4
Lost to follow-up	-	4

Baseline characteristics

Reporting groups	
Reporting group title	MACI
Reporting group description:	
autologous cultured chondrocytes on porcine collagen membrane implant received in previous MACI00206 study	
Reporting group title	Microfracture
Reporting group description:	
Arthroscopic Microfracture treatment received in the previous MACI00206 study	

Reporting group values	MACI	Microfracture	Total
Number of subjects	65	63	128
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)	65	63	128
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Age at the date of informed consent			
Units: years			
arithmetic mean	34.4	32.7	
standard deviation	± 8.94	± 8.80	-
Gender categorical			
Units: Subjects			
Female	25	21	46
Male	40	42	82

Subject analysis sets	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Analysis	

Reporting group values	Safety Analysis Set		
Number of subjects	128		
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)	128		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Age at the date of informed consent			
Units: years			
arithmetic mean	33.6		
standard deviation	± 8.88		
Gender categorical			
Units: Subjects			
Female	46		
Male	82		

End points

End points reporting groups

Reporting group title	MACI
Reporting group description:	
autologous cultured chondrocytes on porcine collagen membrane implant received in previous MACI00206 study	
Reporting group title	Microfracture
Reporting group description:	
Arthroscopic Microfracture treatment received in the previous MACI00206 study	
Reporting group title	MACI
Reporting group description:	
autologous cultured chondrocytes on porcine collagen membrane: Implantation	
Reporting group title	Microfracture
Reporting group description:	
Microfracture: Arthroscopic Microfracture received in the parent study (MACI00206)	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Analysis	

Primary: Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain Scores

End point title	Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain Scores
End point description:	
The KOOS is a validated knee-specific instrument developed to assess the patients' opinion of their knee and associated problems. KOOS consists of 5 subscales: Pain, Function in sports and recreational activities, other Symptoms, Function in activities of daily living (ADL), and knee related Quality of life (QOL). A 5-point Likert scale was used to record the response to each item ranging from 0 (no problems) to 4 (extreme problems). Within each subscale, items were added up and normalized to a value between 0 (extreme problems) and 100 (no problems). Subscales are not combined to calculate a total score. Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain and Function (Sports and Recreational Activities) Scores are pre-specified co-primary end points	
End point type	Primary
End point timeframe:	
MACI00206 Baseline to Week 156	

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	57		
Units: Change of Pain Scores				
arithmetic mean (full range (min-max))	42.14 (-36.1 to 83.3)	35.77 (-2.8 to 83.3)		

Statistical analyses

Statistical analysis title	MANCOVA

Statistical analysis description:

At Week 156 (3 years, co-primary endpoint), the improvement in the MACI group compared with microfracture was analyzed using the MANCOVA model.

Comparison groups	MACI v Microfracture
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	LS Means
Point estimate	6.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.79
upper limit	16.33
Variability estimate	Standard error of the mean
Dispersion value	3.84

Notes:

[1] - Descriptive analysis

Primary: Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Function (Sports and Recreational Activities) Scores.

End point title	Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Function (Sports and Recreational Activities) Scores.

End point description:

The KOOS is a validated knee-specific instrument developed to assess the patients' opinion of their knee and associated problems. KOOS consists of 5 subscales: Pain, Function in sports and recreational activities, other Symptoms, Function in activities of daily living (ADL), and knee related Quality of life (QOL). A 5-point Likert scale was used to record the response to each item ranging from 0 (no problems) to 4 (extreme problems). Within each subscale, items were added up and normalized to a value between 0 (extreme problems) and 100 (no problems). Subscales are not combined to calculate a total score.
Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain and Function (Sports and Recreational Activities) Scores are pre-specified co-primary end points

End point type	Primary

End point timeframe:

MACI00206 Baseline to Week 156

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	57		
Units: Change in function scores				
arithmetic mean (full range (min-max))	45.63 (-20.0 to 95.0)	36.95 (-23.8 to 100)		

Statistical analyses

Statistical analysis title	MANCOVA
Comparison groups	Microfracture v MACI
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS Mean
Point estimate	10.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.23
upper limit	24.13
Variability estimate	Standard error of the mean
Dispersion value	5.49

Secondary: Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain Scores

End point title	Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Pain Scores

End point description:

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	59		
Units: Change in pain scores				
arithmetic mean (full range (min-max))	45.17 (0 to 83.3)	38.42 (-11.1 to 88.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Function (Sports and Recreational Activities) Scores.

End point title	Change From MACI00206 Baseline for the Participant's Knee Injury and Osteoarthritis Outcome (KOOS) Function (Sports and Recreational Activities) Scores.

End point description:

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Change in function scores				
arithmetic mean (full range (min-max))	47.17 (-10.0 to 95.0)	37.56 (-20.0 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Magnetic Resonance Imaging (MRI) Assessments of Degree of Defect Fill

End point title	Magnetic Resonance Imaging (MRI) Assessments of Degree of Defect Fill

End point description:

MRI was assessed by the independent blinded evaluators by means of consensus. The number of participants with a degree of defect fill of >50% is reported.

End point type	Secondary

End point timeframe:

Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	55		
Units: Patient	44	39		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Who Achieve at Least a 10-point Improvement From MACI00206 Baseline in KOOS Pain and Function (Sports and Recreational Activities) Scores

End point title	Proportion of Patients Who Achieve at Least a 10-point Improvement From MACI00206 Baseline in KOOS Pain and Function (Sports and Recreational Activities) Scores

End point description:

A responder is defined as a participant with at least a 10-point improvement in both the KOOS Pain and Function (Sports and Recreational activities) scores from MACI00206 Baseline scores.

End point type	Secondary

End point timeframe:

Up to week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	63		
Units: Patient	51	46		

Statistical analyses

No statistical analyses for this end point

Secondary: The Proportion of Patients in Each Treatment Group Assessed as Treatment Failures

End point title	The Proportion of Patients in Each Treatment Group Assessed as Treatment Failures

End point description:

Patients were considered as a treatment failure if all of the following 5 criteria were met:

Patient's global assessment of their knee joint compared to Baseline was the same or worse
Physician's global assessment of the patient's knee joint compared to Baseline was the same, worse, or significantly worse.
Percent improvement from Baseline in KOOS Pain score was less than 10%.
Physician diagnostic evaluation of failure excluded etiologies (eg, meniscal tear) other than failed treatment of the index lesion.
The physician decided that surgical re-treatment of the index lesion(s) was required that involved either extensive debridement for lesion expansion, violation of the subchondral bone, or ACI.

End point type	Secondary

End point timeframe:

Years 2 through 5 post treatment (MACI or microfracture)

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	63		
Units: Patient	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the Remaining 3 Subscales (Activities of Daily Living) of KOOS

End point title	Change From MACI00206 Baseline in the Remaining 3 Subscales (Activities of Daily Living) of KOOS

End point description:

The KOOS is a validated knee-specific instrument developed to assess the patients' opinion of their knee and associated problems. KOOS consists of 5 subscales: Pain, Function in sports and recreational activities, other Symptoms, Function in activities of daily living (ADL), and knee related Quality of life (QOL). A 5-point Likert scale was used to record the response to each item ranging from 0 (no problems) to 4 (extreme problems). Within each subscale, items were added up and normalized to a value between 0 (extreme problems) and 100 (no problems). Subscales are not combined to calculate a total score.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	59		
Units: Change in Activities of Daily Living Sco				
arithmetic mean (full range (min-max))	42.82 (-8.8 to 82.4)	35.86 (-20.6 to 89.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the Remaining 3 Subscales (Quality of Life) of KOOS

End point title	Change From MACI00206 Baseline in the Remaining 3 Subscales (Quality of Life) of KOOS

End point description:

The KOOS is a validated knee-specific instrument developed to assess the patients' opinion of their knee and associated problems. KOOS consists of 5 subscales: Pain, Function in sports and recreational activities, other Symptoms, Function in activities of daily living (ADL), and knee related Quality of life (QOL). A 5-point Likert scale was used to record the response to each item ranging from 0 (no problems) to 4 (extreme problems). Within each subscale, items were added up and normalized to a value between 0 (extreme problems) and 100 (no problems). Subscales are not combined to calculate a total score.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	59		
Units: Change in QoL Score				
arithmetic mean (full range (min-max))	39.9 (-18.8 to 93.8)	34.53 (-37.5 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the Remaining 3 Subscales (Other Symptoms) of KOOS

End point title	Change From MACI00206 Baseline in the Remaining 3 Subscales (Other Symptoms) of KOOS

End point description:

The KOOS is a validated knee-specific instrument developed to assess the patients' opinion of their knee and associated problems. KOOS consists of 5 subscales: Pain, Function in sports and recreational activities, other Symptoms, Function in activities of daily living (ADL), and knee related Quality of life (QOL). A 5-point Likert scale was used to record the response to each item ranging from 0 (no problems) to 4 (extreme problems). Within each subscale, items were added up and normalized to a value between 0 (extreme problems) and 100 (no problems). Subscales are not combined to calculate a total score.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	57		
Units: Change in Other Symptoms Score				
arithmetic mean (full range (min-max))	32.53 (-7.1 to 78.6)	28.45 (-14.3 to 89.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the Patient's Evaluation of Overall Knee Condition Using the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form

End point title	Change From MACI00206 Baseline in the Patient's Evaluation of Overall Knee Condition Using the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form

End point description:

The IKDC Subjective Knee Evaluation Form is a validated knee-specific measure of symptoms, function,

and sports activity that is appropriate for patients with a wide variety of knee problems. The form consists of 18 items covering the domains of symptoms, functioning during activities of daily living and sports, and current function of the knee.

The IKDC Subjective Knee Evaluation Form is scored by summing the scores for the individual items and then transforming the score to a scale that ranges from 0 to 100. The transformed score is interpreted as a measure of function such that higher scores represent higher levels of function and lower levels of symptoms. A score of 100 is interpreted to mean no limitation with activities of daily living or sports activities and the absence of symptoms.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	59		
Units: Change in IKDC Score				
arithmetic mean (full range (min-max))	35.48 (-11.5 to 80.5)	31.58 (-21.8 to 85.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the Patient's Evaluation of Overall Knee Condition Using the Modified Cincinnati Knee Rating System

End point title	Change From MACI00206 Baseline in the Patient's Evaluation of Overall Knee Condition Using the Modified Cincinnati Knee Rating System

End point description:

The Modified Cincinnati Knee Rating System is a self-assessment of the intensity of sports participation, functional limitations, and the ability to participate in different types of sports. The Modified Cincinnati Knee Rating System overall knee condition score ranges from 1 (poor) to 10 (excellent).

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	59		
Units: Change in MCKR score				
arithmetic mean (full range (min-max))	3.55 (-1.0 to 8.0)	2.71 (-3.0 to 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the 12-Item Short-Form Health Survey (SF-12) Physical Scores

End point title	Change From MACI00206 Baseline in the 12-Item Short-Form Health Survey (SF-12) Physical Scores

End point description:

The SF-12 is a subset of the 36-Item Short–Form Health Survey (SF-36) and includes 8 subscales (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) that are used to calculate the physical (PCS) and mental (MCS) summary component scores.

MCS and PCS are summarized as Z-scores using standard SF-12 scoring and a US population means. The Z-score indicates how many standard deviations a score is from the population mean. Higher values reflect better health. Changes from Baseline are reported.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	55		
Units: Change in SF-12 physical score				
arithmetic mean (full range (min-max))	1.52 (-1.6 to 4.0)	1.28 (-1.3 to 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the European Quality of Life 5 Dimensions (EQ-5D) Visual Analog Scale (VAS) Score

End point title	Change From MACI00206 Baseline in the European Quality of Life 5 Dimensions (EQ-5D) Visual Analog Scale (VAS) Score

End point description:

The EQ-5D is a standardized instrument for use as a measure of health outcome (see the EuroQOL Website for details: www.euroqol.org). Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status. The EQ Visual Analogue Scale (VAS) was used to record the respondents' self-rated health status on a vertical graduated (0-100) VAS where 0 is 'the worst health you can imagine' and 100 is 'the best health you can imagine'.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	58		
Units: Change in VAS scale				
arithmetic mean (full range (min-max))	20.14 (-15.0 to 68.0)	17.1 (-40.0 to 85.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From MACI00206 Baseline in the 12-Item Short-Form Health Survey (SF-12) Mental Component Scores

End point title	Change From MACI00206 Baseline in the 12-Item Short-Form Health Survey (SF-12) Mental Component Scores

End point description:

The SF-12 is a subset of the 36-Item Short–Form Health Survey (SF-36) and includes 8 subscales (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) that are used to calculate the physical (PCS) and mental (MCS) summary component scores.

MCS and PCS are summarized as Z-scores using standard SF-12 scoring and a US population means. The Z-score indicates how many standard deviations a score is from the population mean. Higher values reflect better health. Changes from Baseline are reported.

End point type	Secondary

End point timeframe:

From MACI00206 Baseline to Week 260

End point values	MACI	Microfracture		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	55		
Units: Change in SF-12 Mental score				
arithmetic mean (full range (min-max))	0.38 (-2.2 to 3.3)	0.52 (-2.0 to 3.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Years 2 through 5 post treatment (MACI or microfracture)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	MACI
Reporting group description:	
Patients treated with MACI in the parent study (MACI00206) and consented to participate in the MACI00809 study	
Reporting group title	Microfracture
Reporting group description:	
Treatment received in the parent study (MACI00206) and consented to participate in the MACI00809 study	

Serious adverse events	MACI	Microfracture	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 65 (24.62%)	17 / 63 (26.98%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Salivary gland neoplasm			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cartilage Injury			
subjects affected / exposed	2 / 65 (3.08%)	7 / 63 (11.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft delamination			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus Injury			

subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 65 (1.54%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic injury			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Varicose vein			

subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Retained placenta or membranes			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
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			
Treatment Failure			
subjects affected / exposed	3 / 65 (4.62%)	5 / 63 (7.94%)	
occurrences causally related to treatment / all	3 / 3	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 65 (1.54%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Otosclerosis			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric stenosis			

subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (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			
Osteoarthritis			
subjects affected / exposed	3 / 65 (4.62%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 65 (1.54%)	5 / 63 (7.94%)	
occurrences causally related to treatment / all	1 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			

subjects affected / exposed	1 / 65 (1.54%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament laxity			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone disorder			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint lock			
subjects affected / exposed	0 / 65 (0.00%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint swelling			

subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loose body in joint			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MACI	Microfracture	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 65 (75.38%)	46 / 63 (73.02%)	
Injury, poisoning and procedural complications			
Procedural Pain			
subjects affected / exposed	2 / 65 (3.08%)	5 / 63 (7.94%)	
occurrences (all)	4	5	
Ligament sprain			
subjects affected / exposed	1 / 65 (1.54%)	5 / 63 (7.94%)	
occurrences (all)	1	6	
Cartilage Injury			
subjects affected / exposed	3 / 65 (4.62%)	5 / 63 (7.94%)	
occurrences (all)	3	5	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 65 (16.92%)	13 / 63 (20.63%)	
occurrences (all)	25	28	
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	29 / 65 (44.62%)	32 / 63 (50.79%)	
occurrences (all)	62	61	
Tendonitis			
subjects affected / exposed	4 / 65 (6.15%)	1 / 63 (1.59%)	
occurrences (all)	4	1	
Back Pain			
subjects affected / exposed	3 / 65 (4.62%)	4 / 63 (6.35%)	
occurrences (all)	5	5	
Osteoarthritis			
subjects affected / exposed	2 / 65 (3.08%)	5 / 63 (7.94%)	
occurrences (all)	2	6	
Joint Effusion			
subjects affected / exposed	2 / 65 (3.08%)	5 / 63 (7.94%)	
occurrences (all)	2	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 65 (10.77%)	2 / 63 (3.17%)	
occurrences (all)	20	3	
Influenza			
subjects affected / exposed	4 / 65 (6.15%)	5 / 63 (7.94%)	
occurrences (all)	6	5	

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