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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON36244

Source
ToetsingOnline

Brief title
MACI00809

Condition

- Joint disorders

Synonym
Cartilage defect knee, knee injury

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme
Source(s) of monetary or material Support: Genzyme Europe BV

Intervention

Keyword: Cartilage defect., Extension, MACI Implant, Microfracture

Outcome measures

Primary outcome

Change from MACI00206 Baseline to Week 156 for the patient*s Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain and Function (Sports and Recreational activities) scores.

Secondary outcome

* Change from MACI00206 Baseline to Weeks 24, 36, 52, 78, 104, 208 and 260 for the patient*s KOOS Pain and Function (Sports and Recreational activities) scores.

* Magnetic resonance imaging (MRI) assessments of structural repair parameters at Weeks 52, 104, 156 and 260 including:

o Degree of defect fill based on the thickness of repair tissue; defect fill is to be regarded as the principle MRI indicator of response to treatment

o Degree of integration of the repair tissue with adjacent native cartilage

o Signal intensity of the repair tissue relative to adjacent native cartilage

* Response rate based on KOOS Pain and Function (Sports and Recreational activities) scores: the proportion of patients with at least a 10-point improvement in both the KOOS Pain and Function (Sports and Recreational activities) scores from MACI00206 Baseline at Weeks 24, 36, 52, 78, 104, 156, 208 and 260.

* Treatment failure rate: the proportion of patients in each treatment group assessed as treatment failures at Weeks 24, 36, 52, 78, 104, 156, 208 and 260.

* Average time to treatment failure: the time to treatment failure will be based on the date that the physician decides that surgical re-treatment of the original index lesion is required relative to the date of the original study surgery (i.e., arthroscopy for microfracture and arthrotomy for MACI implant). Treatment failure is only determined in relation to the original treated defect(s).

* Change from MACI00206 Baseline at Weeks 24, 36, 52, 78, 104, 156, 208 and 260 in the remaining 3 subscales of the KOOS instrument .

* Change from MACI00206 Baseline at Weeks 52, 104, 156, 208 and 260 in the

patient*s evaluation of overall knee condition using the Modified Cincinnati Knee Rating System.

* Change from MACI00206 Baseline at Weeks 52, 104, 156, 208 and 260 in the patient*s evaluation of overall knee condition using the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form.

* Change from MACI00206 Baseline at Weeks 52, 104, 156, 208 and 260 in the 12-Item Short-Form Health Survey (SF-12) Acute Version 2.0 for the 8 subscales and the physical and mental summary components.

* Change from MACI00206 Baseline at Weeks 52, 104, 156, 208 and 260 in the European Quality of Life (EuroQOL) 5 dimensions (EQ-5D) health state.

Study description

Background summary

An articular cartilage defect is damage to articular cartilage which may occur from an acute traumatic injury or through progressive mechanical degeneration. They occur along a spectrum of disease and severity. At one end of this spectrum are small, acute lesions that are often diagnosed incidentally at the time of knee arthroscopy, and are not necessarily initially symptomatic. At the other end are larger, more chronic lesions that are often symptomatic and usually do not heal appropriate on their own.
Current treatment algorithms for chondral lesions consider a number of factors including patient demographics, lesion characteristics (eg, size, location, and prior treatment) and overall joint factors (eg, alignment and concurrent pathology) to achieve optimal patient outcomes. Interventions include autologous chondrocyte implantation (ACI), marrow stimulation techniques (MSTs) such as abrasion arthroplasty, drilling and microfracture, and mosaicplasty (also known as osteochondral transplantation). Other treatment options include

knee washout (lavage) with or without debridement.
Matrix-induced autologous chondrocyte implantation (MACI® implant) is an autologous cartilage repair treatment for repair of articular cartilage defects in symptomatic patients, and has been predominantly administered in the knee joint. For this procedure a cartilage biopsy is taken during a surgical procedure, which will be seeded onto a porcine membrane to grow into the MACI Implant product. During e second surgical procedure the product is placed back into the defect.
Genzyme study MACI00206 is a prospective, randomized, open-label, parallel-group, multicenter clinical trial of MACI implant versus arthroscopic microfracture for the treatment of symptomatic articular cartilage defects of the femoral condyle, including the trochlea. The MACI00206 study was designed to build on the clinical experience with MACI implant in the treatment of full-thickness articular cartilage defects compared with microfracture. Additionally, the study assesses the structural cartilage repair generated by MACI implant and microfracture by histological evaluation and magnetic resonance imaging and includes efficacy and safety evaluation up to 2 years post-treatment.
The Committee for Advanced Therapies (CAT) of the European Medicines Agency (EMEA) has recently published a reflection paper on in vitro cultured chondrocyte containing products for cartilage repair of the knee. In this document it is recommended that a 3-year follow-up assessment of clinical efficacy be completed.
This extension study has been designed to examine the 5-year efficacy and safety of MACI implant, compared with arthroscopic microfracture, in patients who received study treatment in the MACI00206 study.

Study objective

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.

Study design

This is an open-label, multicenter, 3-year extension study for patients who received study treatment (MACI implant or microfracture) in the MACI00206 study. Patients will have until the end of the visit window for the last visit of this extension study (Week 260 + 6 weeks) to consent to enter this extension study; written informed consent is required prior to enrollment in the study.
Efficacy and safety assessments will be performed at scheduled visits 3, 4 and 5 years following treatment in MACI00206 (i.e., at Weeks 156, 208 and 260 post-arthrotomy for patients treated with MACI implant or at Weeks 156, 208 and 260 post-arthroscopy for patients treated with microfracture). Patients*

MACI00206 data will be utilized for statistical analysis (e.g., for treatment failure analysis) in this extension study.
Patients withdrawn from the MACI00206 study prior to their scheduled Week 104 visit and enrolled into the MACI00809 study will have their remaining scheduled assessment (from the MACI00206 study) within the MACI00809 study in addition to the assessments mentioned for Weeks 156, 208 and 260. Note that data for any visits for which the visit window has passed will not be collected and will be considered
missing.
Any patient requiring surgical re-treatment of the treated defect(s) and meeting other specific criteria relating to changes in the condition of the treated knee joint will be considered a treatment failure and may be asked to attend an unscheduled visit for treatment failure evaluation. Patients who are considered treatment failures may receive appropriate alternative treatment, at the discretion of the Investigator, which may include MACI implant.
Additionally, patients who do not meet the specific treatment failure criteria as defined in this protocol but require re-treatment in the opinion of both the Investigator and the Treatment Failure Evaluation Committee, may also receive re-treatment which may include MACI implant. All patients requiring re-treatment with MACI implant will receive
MACI as investigational product provided for rescue treatment. Patients determined to be treatment failures will not be withdrawn from this extension study.

Intervention

Patients are asked to completed questionnaries during the follow up visits 3, 4 and 5 years following treatment in MACI00206 (ie, at Weeks 156, 208 and 260 post-arthrotomy for patients treated with MACI implant or at Weeks 156, 208 and 260 post-arthroscopy for patients treated with microfracture).
In addition Magnetic resonance imaging (MRI) assessments of structural repair parameters at Weeks 156 and 260 following treatment in MACI00206 will be made.

Patients withdrawn from the MACI00206 study prior to their scheduled Week 104 visit and enrolled into the MACI00809 study will have their remaining scheduled assessment from the MACI00206 study within the MACI00809 study in addition to the assessments mentioned for Weeks 156, 208 and 260. Patients who are considered treatment failures may be asked to attend an unscheduled visit for treatment failure evaluation.

Study burden and risks

Although the patient will not receive any further treatment as part of this study they may be retreated if needed. The investigator will assess improvement using appropriate evaluations and will discuss the retreatment possibilities with the patient. These may include, but are not limited to, MACI implant or

microfracture. There may be other side effects or discomforts from your retreatment in this study (if applicable) that are not yet known.
Risks involved with retreatment by MACI implant: If the patient is retreated with MACI implant, the cartilage defect will be treated with a surgical implant consisting of their own live cartilage cells (obtained during the MACI00206 study) on a collagen membrane. As with any surgical implant, there are risks of infection, failure of implant fixation, and/or failure to relieve your symptoms. In earlier clinical trials with MACI implant, very few reactions have been identified as causally related to MACI implant. These reactions included overgrowth of the implanted cartilage tissue, or separation of the membrane from the defect site (either complete or partially, possibly leading to loose bodies in the joint).

Possible risks involved with MRI: Interference with internal devices. Patients will be asked if they have any internal device or implant such as a heart pacemaker, metal pins or a medication pump.

Reproductive risks:
A female patient or a female partner of the patient who becomes pregnant, is strongly recommended by Genzyme to immediately inform the study doctor. When the patient or the female partner agrees, follow up information concerning the pregnancy and the outcome can be obtained and shared with Genzyme.

Benefit:
there may not be direct medical benefits for the patients. However, we hope the information learned from this study will benefit other patients with cartilage defects in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients must meet the following criteria to participate in this extension study:;1. Received study treatment (MACI implant or microfracture) in the MACI00206 study.;2. Provides written informed consent.

Exclusion criteria

Exclusion Criteria, not applicable for this extension study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2011
Enrollment:	58
Type:	Actual

Ethics review

Approved WMO Date:	20-09-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-03-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-05-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	22-11-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-02-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-08-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-08-2015
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-016970-33-NL
ClinicalTrials.gov	NCT01251588
CCMO	NL32974.041.10