Randomized controlled trial on clinical outcomes and safety of Instant MSC Product accompanying Autologous Chondron Transplantation (IMPACT) for focal articular cartilage lesions of the knee

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This study has been transitioned to CTIS with ID 2024-514612-27-01 check the CTIS register for the current data. The primary objective is to measure the level of clinical improvement and quality of life at 3, 6 and 9 months compared to...

Ethical review	Approved WMO
Status	Completed
Health condition type	Tendon, ligament and cartilage disorders
Study type	Interventional

Summary

ID

NL-OMON55402

Source
ToetsingOnline

Brief title
IMPACT2

Condition

- Tendon, ligament and cartilage disorders

Synonym
cartilage defect/ cartilage lesion

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: cartilage defect, knee, MSCs and Chondrons, one stage cartilage transplantation

Outcome measures

Primary outcome

The primary objective is to measure the level of clinical improvement and

quality of life at 3, 6, and 9 months compared to conservative treatment. This

is assessed by, subscales of, the KOOS and the EQ5D, respectively

Secondary outcome

The secondary objective is to measure functional repair using MRI at 6 and 18

months postoperative

Study description

Background summary

Articular cartilage defects in the knee have poor intrinsic healing capacity and may lead to functional disability and osteoarthritis. Cartilage cell therapy using autologous chondrocyte implantation has been established as the first advanced treatment therapy medicinal product. Although this technique has achieved good midterm results, it is a costly and extensive twostage procedure which is limited by the number of chondrocytes obtained by biopsy and the dedifferentiation resulting from the expansion phase. Therefore, it was withdrawn from the European Market. There is a highly unmet need for treatment of articular cartilag defect. A new cartilage repair technique should aim at decreasing surgical trauma, lowering complexity, improving logistics and costeffectiveness while retaining or improving clinical outcome. Direct contact between mesenchymal stromal cells (MSCs) and dedifferentiated articular chondrocytes in vitro showed improvement of the chondrogenic phenotype of

dedifferentiated articular
chondrocytes. In addition, preserving the pericellular matrix of chondrocytes improves cartilage formation. These chondrons (chondrocytes with their pericellular matrix) have shown improved cartilage formation when combined with MSCs. These cells can be mixed with a widely used, commercially available, fibrin cell carrier and applied to the cartilage lesion within one surgical procedure, using a minimally invasive and eventually arthroscopic technique. In a phase I-II trial, we have shown that immediate transplantation of a potent cellbased cartilage product is safe, reduces patient morbidity and improves patient care. Therefore, we now propose the clinical evaluation in a phase II-III randomized monocenter study of IMPACT for treatment of articular cartilage defects of the knee to prove clinical safety and feasibility.

Study objective

This study has been transitioned to CTIS with ID 2024-514612-27-01 check the CTIS register for the current data.

The primary objective is to measure the level of clinical improvement and quality of life at 3, 6 and 9 months compared to conservatively treated patients. The secondary objective is to measure functional repair using MRI at 6 and 18 months postoperative.

Other important objectives are clinical safety and healthcare use and costs related to the procedure as well as the healthrelated work leave during the study period.

Study design

This is a phase III randomized controlled trial, comparing efficacy and safety of a new ATMPproduct for isolated articular cartilage lesions to standard care (conservative treatment). After 9 months patients in the control group are allowed to cross over and receive IMPACT treatment.

Intervention

Onestage surgery using the Instant MSC Product accompanying Autologous Chondron Transplantation (IMPACT)

Study burden and risks

Potential risks: graft failure and/ or migration or foreign body responce, tissue hypertrophy (excessive growth of new tissue), and general knee surgery related risks such as surgical site infection, arthralgia, joint crepitation, swelling, effusion, chondropathy, synovitis, deepvein thrombosis, pulmonary embolism, haemarthrosis and arthrofibrosis. See section

7.2 for definitions of AEs. At this moment, this is the only (therapeutic) treatment option. The only alternative is physical therapy, which does not lead to repair of the cartilage defect

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Provides written informed consent, is able to understand the content of the study, understands the requirements for follow-up visits and is willing to provide the required information at follow-up visits and in the questionnaires.
- Symptomatic articular cartilage lesion of the knee (femoral condyles or trochlea).
- Age 18 to 45 years old
- Modified Outerbridge Grade III or IV isolated cartilage lesion of the knee.

- A post-debridement size of the cartilage lesion > 2cm2 and <= 8 cm2
- At least 50% of functional meniscus remaining. Meniscal repair or resection is allowed during the IMPACT surgery provided that the surgeon is able to confirm that at least 50% of functional meniscus remains.
- Stable knee ligaments (i.e. anterior and posterior cruciate ligaments).

Exclusion criteria

- Malalignment of >5 degrees
- (History of) osteoarthritis, defined as Kellgren-Lawrence grade >3 as determined from appropriate X-ray.
- Concomitant inflammatory disease that affects the joint (rheumatoid arthritis, metabolic bone disease, psoriasis, gout, symptomatic chondrocalcinosis)
- (History of) Septic arthritis.
- (History of) Total menisectomy in the target knee joint.
- Any surgery in the knee joint for cartilage treatment, 6 months prior to study inclusion.
- Risk groups for MRI scanning due to the magnetic field like patients with pacemakers, nerve stimulators, metal particles, stents, clips or implants, (possible) pregnancy or breast feeding.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	23-07-2019

Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	10-10-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-05-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-05-2021

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-01-2022
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
EU-CTR	CTIS2024-514612-27-01
EudraCT	EUCTR2018-003470-27-NL
CCMO	NL67161.000.18