Prospective feasibility, non-randomized, single arm multicentre, multinational interventional clinical investigation using INSTRUCT therapy for the repair of knee cartilage defects.

Published: 31-08-2010
Last updated: 04-05-2024

This pilot clinical trial has been designed to evaluate the safety and performance of the INSTRUCT scaffold, and to collect preliminary efficacy data

Ethical review	Not approved
Status	Will not start
Health condition type	Bone and joint injuries
Study type	Interventional

Summary

ID

NL-OMON34984

Source
ToetsingOnline

Brief title
INSTRUCT study

Condition

- Bone and joint injuries

Synonym
cartillage damage, traumatic knee cartillage defect

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cartillagerepair, knee, scaffold

Outcome measures

Primary outcome

The safety of the device will be evaluated looking at the incidence of :

- Device related adverse events during the healing period and up to 3 months

follow up

(Adverse device effects).

- Process related adverse events as observed intra-operatively and up to 3

months follow up

- Adverse events related to the surgical procedure specific to the device

implantation.

- Long term adverse device effects as observed from the period 3-24 months

Performance of the device has been defined as mechanical support of the

biodegradable PolyActive

scaffold observed as lesion filling at implantation shown by 3 months MRI,

compared to filling at

discharge.

Secondary outcome

Incidence of non-related treatment-emergent (serious) adverse events throughout

the 24 months of the

clinical investigation.

- Validation of timing of biopsy allowingpreliminary efficacy determination

- Preliminary efficacy:

o Improved KOOS, IKDC and painVAS scores

o Presence of cartilage formationas shown by biopsy at 6 or 12 months follow up

and by dGEMRIC MRI at 6, 12 and 24months follow-up

User handling feedback (complications and technical challenges):

- Ease of use of the device, instrumentation and process prior to and during

cell processing.

- Ease of use of device and instrumentation at implantation.

- Complaints (other than adverse events) and/or recommendations related to the

device, instrumentation and process.

Health economic data:

- Duration of the intra-operative procedure.

- Duration of hospital stay.

- Duration of rehabilitation program.

Study description

Background summary

This pilot clinical investigation is intended to provide sufficient data to confirm that the INSTRUCT therapy is safe and performs as a treatment for cartilage repair in view of obtaining the CE-mark. The clinical investigation will also provide on the first 10 subjects a subset data on the validity of the timepoint at which efficacy endpoints can be observed. The subject population included in this nonrandomized clinical investigation is not intended to provide statistically significant data on efficacy but will provide a preliminary confirmation on the clinical safety and performance results prior to starting a more extensive randomized clinical investigation to confirm longer term efficacy data.

Study objective

This pilot clinical trial has been designed to evaluate the safety and performance of the INSTRUCT scaffold, and to collect preliminary efficacy data

Study design

This multicenter, multinational non-randomized prospective interventional feasibility clinical investigation, shall be conducted in initially 2-3 (first 10 subjects) and thereafter in 5-6 (subsequent 30 subjects) investigation sites in Europe.
This clinical investigation has been designed primarily to confirm safety and performance of the device to support design dossier approval in Europe. The safety and performance of the material of the INSTRUCT scaffold has been confirmed through extensive testing and a wide use in the orthopaedic area by Isotis* product Synplug. Synplug is also approved in the US through a 510K procedure for the use of cement restriction. Hence, this clinical investigation is designed to provide clinical data for the use a specific autologous cell processing and seeding of cells on the PolyActive scaffold as a treatment for cartilage defects.
The first 3 subjects will undergo a biopsy at 6 month follow up to confirm whether at this stage the formation of hyaline-like cartilage can be observed. If the results of histopathology are positive meaning hyaline-like cartilage was observed, then the biopsy will continue to be performed on the

remainder of the subjects at 6 months. Should histopathology fail to show hyaline-like cartilage at 6
months then the biopsy for all subsequently enrolled subjects shall be performed at 12 months follow
up. The first 3 subjects however will not undergo a second biopsy at 12 months as part of this clinical
investigation.
After the treatment of the first 10 subjects a first safety interim observation shall be performed. Upon
absence of serious adverse device effects during surgery, further enrolment of additional 30 subjects
shall be performed in a larger number of investigation sites.
After 10 subjects have reached 3 months follow up, an interim analysis for safety and performance
shall be performed

Intervention

During one surgical procedure, the following procedures take place: Bone marrow biopsy, Cartilage biopsy, blood sample,
implantation of scaffold with cells.

Study burden and risks

Most of the risks associated with the INSTRUCT scaffold and procedure are those associated with any surgical procedure or with alternative cartilage repair therapies.
Some adverse events of interest have been identified and will be reported in an expedite way during the study (similarly to SAEs) : surgical site inflammation, surgical site infection, foreign body response, migration or dislocation of the scaffold, graft delamination, haemarthrosis and knee locking. More details can be found in section 16.4 of the Clinical Investigation Plan.

A process and product risk analysis according to ISO 14971 Application of risk management to medical devices has been conducted. Risks have been proven minimized or eliminated through appropriate design control, confirmed by pre-clinical bench, laboratory and animal testing. This pilot clinical investigation is conducted to make final conclusions about the safety of the device and its related processes.

The following benefits are expected from the INSTRUCT treatment:
• Reduced pain after the surgery
• Improved mobility
• Reduced need for additional knee surgeries
• Reduced cartilage damage and development of osteoarthritis.

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

1. Subjects aged 18-50 years old, (skeletally mature as shown by epiphyseal plate).
2. Subject is able/willing to provide written informed consent and willing to comply with all pre-per and post operative clinical investigation requirements.
3. Subjects presenting a single symptomatic unilateral knee traumatic cartilage lesion of the femoral condyle grade III to IV (Outerbridge grading system)a
4. Subjects with a single lesion of the femoral condyle with dimension after

debridement between - 1 cm2 and - 2.6 cm2. (length/diameter of the lesion between 1.3 cm and 1.8 cm)
5. Subjects agree to participate in a strict rehabilitation protocol and follow-up.

Exclusion criteria

1. Subjects who are participating in any concurrent investigation.
2. Subjects with presence of more than one clinically relevant cartilage lesion on the femoral condyle.
3. Subjects with presence of a clinically relevant cartilage lesion on the patella.
4. Female subjects who are pregnant or lactating at baseline, or female subjects who plan to become pregnant during the course of the study.
5. Subject is presenting with any knee defect on the other leg which may interfere with the post operative rehabilitation process.
6. Subjects with varus or valgus malalignment exceeding 5°
7. Subjects with ligamentous instability of the knee unless resolved by reconstruction of the cruciate-ligaments within the 6 months prior to enrolment.
8. Subjects with a history of autoimmune disease.
9. Subjects suffering from advanced osteoarthritis, rheumatoid arthritis, gout or recurrent episodes of pseudo-gout, septic arthritis, inflammatory joint disease, Paget disease of bone, ochronosis, acromegaly, hematochromatosis, Wilson disease, primary osteochondromatosis, heritable disorders, collagen gene mutations.
10. Subjects suffering from osteomyelitis.
11. Subjects who have undergone a meniscal transplant.
12. Subjects with a present (or previous if not resorbed) meniscal suture
13. Subjects who underwent any surgery or

other local treatment to the affected knee within the past 6 months, other than specified in exclusion criterion 7.
14. Subjects who underwent a meniscal resection resulting in remaining lateral and medial meniscal tissue volume of < 50%.
15. Subjects with tibial defects.
16. Subjects who received hyaluronic acid intra-articular injections into the affected knee within the past 6 months prior to enrolment.
17. Subjects who received corticosteroid therapy either systemically (PO or IM) or intra-articularly in the affected knee within 6 months prior to enrolment.
18. Subjects taking medications or having treatments which are known to have an effect on bone/cartilage formation such as but not limited to chemotherapy and immunosuppressive drugs.
19. Subjects with a known allergy to penicillins, to gadolinium (or derived contrast agents) or multiple severe allergies.
20. Subjects suffering from obesity (body mass index of >30).
21. Subjects with vascular or neurological disease affecting lower limbs.
22. Subjects with uncontrollable diabetes
23. Subjects with chronic severe renal insufficiency or with renal dysfunction
24. Subjects with a history of kidney disease or kidney transplantation
25. Subjects suffering from painful or disabling disease of the spine, hips or lower limbs that could interfere with the evaluation or rehabilitation of the target knee.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Generic name:	INSTRUCT scaffold
Registration:	No

Ethics review

Not approved

Date:	31-08-2010
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

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
ClinicalTrials.gov	NCT01041885
CCMO	NL33221.094.10