A multi-center, pivotal, non-randomized, prospective, open-label study to evaluate the safety and performance of the Hy2Care Injectable Hydrogel for the repair of cartilage defects in the knee.

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Primary objectives:Safety:To demonstrate the safety of the investigational device in 10 subjects at 3 months post-surgery.Safety cohort data will be pooled with the performance cohort data, to measure the performance and safety of the...

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

Summary

ID

NL-OMON50832

Source
ToetsingOnline

Brief title
ACTIVE

Condition

- Tendon, ligament and cartilage disorders
- Bone and joint therapeutic procedures

Synonym
Cartilage defect, cartilage lesion

Research involving
Human

Sponsors and support

Primary sponsor: Hy2Care B.V.
Source(s) of monetary or material Support: Hy2Care B.V.

Intervention

Keyword: Cartilage defect, Cartilage regeneration, Cartilage treatment, Hydrogel

Outcome measures

Primary outcome

Safety:

• Incidence, nature and severity of procedure and/or device related adverse events up to 3 months post-surgery.

Performance:

• Change from baseline in the composite (average of the 5 subscales) KOOS at 12 months post-surgery.

Secondary outcome

The following secondary outcome measures will be captured during both the safety and performance phases of the study:

Imaging measures:

• Determine the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) II score at 12, 24 and 60 months post-surgery.

Patient reported outcome measures:

• Change from baseline in the composite KOOS at 3 and 6 months post-surgery .

• Change from baseline in the KOOS subscale scores (pain, other symptoms,

function in daily living, function in sport and recreation and knee related quality of life) at 3-, 6-, 12-, 24-, 36-, 48-, and 60 -months post-surgery .

• Change from baseline in the EuroQol-5-dimension-5L (EQ-5D-5L) health questionnaire at 3-, 6-, 12-, 24-, 36-, 48-, and 60 -months post-surgery .

• Change from baseline in health-related quality of life as measured by the 36-Item Short-Form Health Survey version 2 (SF-36) scores at 3-, 6-, 12-, 24-, 36-, 48-, and 60 -months post-surgery .

• Change in the Numeric (pain) Rating Scale (NRS) score from baseline at the following time-points post-surgery 1 day, 1 week, 1-, 3-, 6-, 12-, 24-, 36-, 48-, and 60 -months post-surgery .

Physical impairment measures:

• Knee range of motion (ROM) at 1, 3, 6 and 12 months post-surgery.

Other measures:

• Ease of use by surgeons, as measured with a VAS rating scale .

• Proportion of patients requiring further intervention or treatment to the affected knee during the 12-month follow-up period.

Study description

Background summary

The Hy2Care Injectable Hydrogel is a two-component injectable and bioresorbable hydrogel intended for treatment of cartilage defects in the knee. The hydrogel is composed of a mixture of natural polymer conjugates that are mixed intra-operatively and which cross-link in situ by means of a mild enzymatic

reaction. The product aims at functional repair of cartilage defects in the human knee and regeneration of cartilage.
After injection of the liquid gel in the cartilage defect, and polymerization, the hydrogel adheres to the surrounding tissue structures with use of a primer. Its principle of operation is (temporary) filling of the chondral defect and providing a scaffold structure, allowing perilesional developing chondrocytes to migrate into and attach to the defect (and gel), eventually proliferating into hyaline-like regenerated cartilage.
Currently, some other injectable liquid gels are available on the market/used in the clinic. However, none of these gels consist of the same components/are formed in a similar way as the Hy2Care Injectable Hydrogel. Furthermore, principle of operation of most of these products is different, in the sense that they are mostly combined with bone marrow stimulating procedures such as micro-fracturing. Therefore, both the working principle and the *design* (key functional elements) can be considered novel features as compared to existing products.

Study objective

Primary objectives:
Safety:
To demonstrate the safety of the investigational device in 10 subjects at 3 months post-surgery.
Safety cohort data will be pooled with the performance cohort data, to measure the performance and safety of the investigational device.

Performance:
To demonstrate the safety and performance of the investigational device based on functional outcome measures in a larger number of patients at 12, 24 and 60 months post-surgery.

Secondary objectives:
• To demonstrate the safety and performance of the investigational device based on magnetic resonance imaging and physical outcome parameters up to 60 months post-surgery,
• To evaluate surgeon satisfaction and ease of use of the investigational device by means of a questionnaire.

Study design

This is a multi-center, pivotal, non-randomized, prospective, open-label clinical investigation.
Safety oversight throughout will be provided by an independent Data Monitoring Committee (DMC) comprised of a clinical expert (knee surgeon), medical monitor and a senior statistician.
The clinical investigation will be split into two cohorts:

Safety cohort: The safety cohort is intended to determine the primary safety of the investigational device. In this cohort, 10 subjects will be treated at preferably 1 site: UMC Utrecht. The safety cohort will receive the investigational device intraoperatively.
Following implantation of the investigational device in the initial safety cohort, the DMC will continuously monitor all emerging safety issues against the defined stopping rules of the clinical investigation. Any treatment-emergent severe adverse events or other safety concerns during the safety phase of the clinical investigation will immediately be referred, on a case by case basis, to the DMC for review against the stopping rules.
A formal review of safety against the stopping rules will be undertaken by the DMC when all of the safety cohort patients reach 3 months post-surgery.
Subjects will be followed post-operatively for 60 months. The subjects in the safety cohort will undergo the same procedures as in the performance cohort, therefore all data acquired for the safety cohort will also be used to measure the performance and safety endpoints defined for the performance cohort.
Performance cohort: The performance cohort is intended to demonstrate the safety and performance of the investigational device. This cohort will be initiated after the completion of the safety phase and approval from the DMC.
In the performance cohort 36 subjects will be treated at up to 5 investigational sites, where they will receive the investigational device intraoperatively.
The sample size has been calculated based on a minimal clinically important change (MIC) of 10 points in the composite Knee Injury and Osteoarthritis Outcome Score (KOOS, a patient reported outcome measure), compared to baseline, to provide an assessment of the performance of the investigational device. The primary endpoint is at 12 months follow-up. All subjects will be followed post-operatively for 60 months. Additional assessments occur at 1, 3, 6, 12, 24, 36, 48 and 60 months.

Intervention

Knee surgery using the Hydrogel to fill the defect.

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, deep-vein thrombosis, pulmonary embolism, haemarthrosis and arthrofibrosis.

Contacts

Public
Hy2Care B.V.

Drienerlolaan 5 ZH143
Enschede 7522 NB
NL
Scientific
Hy2Care B.V.

Drienerlolaan 5 ZH143
Enschede 7522 NB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Subject is at least 18 years and maximum 50 years of age at time of consent;
2. Subject presents with a symptomatic defect in the knee with an NRS pain score of 4 or more;
3. Subject presents with defect(s) in the knee cartilage with ICRS classification grades IIIa or IIIb;
4. Subject has a contained lesion(s) of between 0.5 - 2 cm2 in size, and it is localized on the femoral condyle or trochlea; if there are multiple defects, the sum of all sizes should not be more than 2 cm2;;
5. Subject has an intact (ICRS grade <= 1) articulating joint surface (without *kissing lesions*);
6. Subject is willing and able to comply with all aspects of the treatment, including MRI, after-care rehabilitation and evaluation schedule over a 60-month duration; and

7. Subject is willing and able to provide documented Ethics Committee-approved informed consent prior to initiation of any study procedures.

Exclusion criteria

1. Subject has a BMI > 30 kg/m2;
2. Subject underwent index-knee surgery < 3 months prior to study treatment.
3. Subject suffers from any medical condition that would hinder cartilage repair, such as additional unresolved comorbidities related to the index knee:
a. Untreated anterior cruciate ligament (ACL) and/or posterior cruciate ligament (PCL) deficiency or,
b. Complex ligamentous instability of the knee/ insufficient ligament support,
c. Meniscus lesions, total or partial (more than 1/2 of total volume) resected meniscus,
d. Limited joint mobility (flexion less than 110 degrees),
e. Untreated varus/valgus joint malalignment of more than 5 degrees,
f. Subject has a trochlear cartilage defect that is associated with (suspected) patella maltracking without surgical correction;
g. Subject underwent previous (failed) cartilage repair procedure(s), such as microfracture (MF),
Osteochondral Autograft Transplantation (OATS) or Autologous Chondrocyte Implantation (ACI) with or without use of a scaffold (matrix) in the index knee.
4. Subject has (history of) generalized osteoarthritis, defined as Kellgren-Lawrence grade >1 as determined from recent (<6 months at time of enrollment) X-ray;
5. Subject suffers from inflammatory joint diseases (e.g. rheumatoid arthritis, Bechterew disease, chondromatosis);
6. Subjects suffers from autoimmune disease, vascular or neurological disease;
7. Subject suffers from an active or recent local or systematic infection, or has a history of knee infections;
8. Subject has an active malignant tumor at the time of treatment;
9. Subject has hypersensitivity or allergy to the constituents of the product.
10. Pregnant or lactating women at the time of enrollment or women who are planning to become pregnant during the duration of the study.

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-03-2022
Enrollment:	46
Type:	Actual

Medical products/devices used

Generic name:	Surgically Injectable Hydrogel
Registration:	No

Ethics review

Approved WMO Date:	18-01-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-01-2025
Application type:	Amendment

Review commission: METC NedMec

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
CCMO	NL76283.000.21