Spheroids of human autologous matrix-associated chondrocytes (Chondrosphere) for articular cartilage defects

SUMMARY

Spheroids of human autologous matrix-associated chondrocytes are intended to be used as therapy for articular cartilage defects. If licensed, this technology will provide an additional treatment option for this patient group. Spheroids of human autologous matrix-associated chondrocytes are formed from the patient’s own undamaged articular condyles. Chondrocytes are harvested from healthy articular cartilage, cultivated for 8-10 weeks \textit{in vitro}, and condensed into spheroids (chondrospheres). The 3-dimensional spheroids are then transplanted into the defect. Spheroids of human autologous matrix-associated chondrocytes are licensed in Germany for the treatment of articular cartilage defects of the knee, hip, shoulder, elbow and ankle.

Articular cartilage damage in the knee may be caused by acute injury, often as a result of a sporting activity. Long-term, damage to the articular cartilage can lead to osteoarthritis, and in some cases, knee replacement with an artificial joint is required. There are no reliable estimates of the prevalence of symptomatic articular cartilage defects of the knee, although an estimated 10,000 people have cartilage damage serious enough to require treatment in the UK every year. The number of people with symptomatic cartilage defects suitable for autologous chondrocyte implantation is estimated to be between 200 and 500 per year in the UK.

Current treatment options include analgesics for relief of symptoms, knee lavage, and procedures to re-establish the articular surface, such as marrow stimulation techniques, mosaicplasty, and autologous chondrocyte implantation. Spheroids of human autologous matrix-associated chondrocytes are currently in phase III clinical trials comparing their effect on the Knee Injury and Osteoarthritis Outcome Score (KOOS) against microfracture therapy.
TARGET GROUP

• Patients with articular cartilage defects, initially of the knee, but the company report that the anticipated licence may potentially also include the hip, shoulder, elbow and ankle.

TECHNOLOGY

DESCRIPTION

Spheroids of human autologous matrix-associated chondrocytes (Chondrosphere; ACT3D-CS) are formed from the patient’s own undamaged articular condyles. Chondrocytes are harvested from healthy articular cartilage, cultivated for 8-10 weeks in vitro, and condensed into spheroids (chondrospheres). The 3-dimensional spheroids are then transplanted into the defect. In clinical trials, the recommended dose of spheroids of human autologous matrix-associated chondrocytes was 10-70 spheroids/cm².

Spheroids of human autologous matrix-associated chondrocytes are licensed in Germany for the treatment of articular cartilage defects of the knee, hip, shoulder, elbow and ankle.

INNOVATION and/or ADVANTAGES

If licensed, spheroids of human autologous matrix-associated chondrocytes for articular cartilage defects will provide an additional treatment option for this patient group.

DEVELOPER

Co.don.

AVAILABILITY, LAUNCH OR MARKETING

The company submitted a Marketing Authorisation Application to the EMA in Q4 2012.

PATIENT GROUP

BACKGROUND

Articular cartilage refers to hyaline cartilage on the articular surfaces of bone, which provides a smooth and resilient surface, allowing virtually frictionless movement within the knee joint. Cartilage has no blood vessels and therefore has very limited ability to repair itself. Articular cartilage damage in the knee can be caused by acute injury, often as a result of a sporting activity, or it may arise without obvious trauma in individuals with defective cartilage. Damage to the articular cartilage is associated with symptoms such as knee pain, knee swelling, knee locking and giving way of the knee joint. Long-term, this can lead to osteoarthritis, and in some cases a knee replacement with an artificial joint is required.

NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to:

• The National Service Framework for long-term conditions. 2005.

**CLINICAL NEED and BURDEN OF DISEASE**

There are no reliable estimates of the prevalence of symptomatic articular cartilage defects of the knee, although an estimated 10,000 people have cartilage damage serious enough to require treatment in the UK every year\(^3\). The number of people with symptomatic cartilage defects suitable for autologous chondrocyte implantation is estimated to be between 200 and 500 people per year in the UK\(^3\).

**PATIENT PATHWAY**

**RELEVANT GUIDANCE**

**NICE Guidance**


**Other Guidance**

• American Physical Therapy Association. Knee pain and mobility impairments: meniscal and articular lesions. Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the American Physical Therapy Association. 2010\(^6\).

**CURRENT TREATMENT OPTIONS**

Current treatment options include analgesics for relief of symptoms, knee lavage with or without debridement (removal of damaged cartilage), and procedures to re-establish the articular surface\(^3\)\(^,\)\(^a\). Interventions that aim to re-establish the articular surface include\(^3\)\(^,\)\(^a\):

- Marrow stimulation techniques (abrasion arthroplasty, drilling and microfracture)
- Mosaicplasty (osteochondral transplantation)
- Autologous chondrocyte implantation (ACI), e.g. ChondroCelect; MACI; unbranded ACI
- Osteotomy (rare in young patients [those aged 18-40]\(^a\))
- Knee replacement (rare in young patients\(^a\)).

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\(^a\) Expert personal opinion.
## EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT01222559, cod16HS13, 2009-016466-82; spheroids of human autologous matrix-associated chondrocytes vs microfracture; phase III.</th>
<th>NCT01225575, cod 16HS14, 2009-016816-20; spheroids of human autologous matrix-associated chondrocytes; phase II.</th>
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</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Co.don</td>
<td>Co.don.</td>
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<tr>
<td>Status</td>
<td>Ongoing.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry¹.</td>
<td>Trial registry¹.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (not UK).</td>
<td>EU (not UK).</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised; active-controlled.</td>
<td>Randomised.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=150 (planned); aged 18-50 years; ICRS grade III or IV single defect chondral lesions on femoral condyles; 1-4cm² after debridement to healthy cartilage, ≤6mm in depth.</td>
<td>n=75 (planned); aged 18-50 years; ICRS grade III or IV single defect on medial or lateral femoral condyle, trochlea, tibia or retropatellar defects; 4-10cm² after debridement to healthy cartilage, ≤6mm in depth.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to spheroids of human autologous chondrocytes, at 10-70 spheroids/cm²; or microfracture.</td>
<td>Randomised to spheroids of human autologous chondrocytes, at 3-7, 10-30, or 40-70 spheroids/cm².</td>
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<tr>
<td>Follow-up</td>
<td>Up to 5 years follow-up.</td>
<td>Up to 5 years follow-up.</td>
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<tr>
<td>Primary outcome/s</td>
<td>Knee injury and osteoarthritis outcome score (KOOS).</td>
<td>KOOS.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>MOCART¹ (MRI score); arthroscopy and biopsy; ICRS visual histological assessment score; Bern score⁴; IKDC; Lysholm score; absence from work; safety.</td>
<td>MOCART (MRI score); arthroscopy and biopsy; ICRS visual histological assessment score; Bern score; IKDC; Lysholm score; absence from work; safety.</td>
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<tr>
<td>Expected reporting date</td>
<td>Q4 2016.</td>
<td>Q2 2015.</td>
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</tbody>
</table>

## ESTIMATED COST and IMPACT

### COST

The cost of spheroids of human autologous chondrocytes for cartilage defects is not yet known.

### IMPACT - SPECULATIVE

**Impact on Patients and Carers**

- Reduced mortality/increased length of survival
- Reduced symptoms or disability
- Other:
- No impact identified

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¹ International Cartilage Repair Society clinical cartilage evaluation system.
² Magnetic Resonance Observation of Cartilage Repair Tissue
³ Assessment of cartilage repair success.
⁴ International Knee Documentation Committee score
⁵ Tegner Lysholm Knee Scoring Scale – assesses how knee pain affects quality of life.
Impact on Health and Social Care Services

- Increased use of existing services: procedure required to harvest chondrocytes for transplantation
- Decreased use of existing services: may be potential for reduced need for other operative procedures, but this is untested at present.
- Re-organisation of existing services
- Need for new services
- Other: None identified

Impact on Costs and Other Resource Use

- Increased drug treatment costs
- Reduced drug treatment costs
- Other increase in costs.
- Other reduction in costs:
- Other: uncertain unit cost compared to existing treatments
- None identified

Other Issues

- Clinical uncertainty or other research question identified: unknown long-term efficacy.
- None identified

REFERENCES