

National Horizon Scanning Centre

ChondroCelect for knee cartilage defects

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This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

ChondroCelect for knee cartilage defects

Target group

- Knee cartilage defects.

Technology description

ChondroCelect is a somatic cell therapy product developed from autologous cartilage-forming cells or chondrocytes, expanded *ex vivo* prior to implantation. ChondroCelect allows formation of stable cartilage *in vivo*, and a durable repair of cartilage defects. ChondroCelect is based on an optimised cell culturing process, which aims to avoid de-differentiation and/or maintain the differentiated phenotype of cultured chondrocytes.

ChondroCelect is administered to patients as part of an autogenous cartilage implantation (ACI) procedure. The combination of ChondroCelect (the product) and ACI (the procedure) is called Characterised Chondrocyte Implantation (CCI™). The process consists of steps performed over 4 to 6 weeks:

1. An arthroscopy to assess the cartilage lesion macroscopically and to take a biopsy from a lesser weight-bearing area of the joint.
2. Cells are harvested from the cartilage biopsy for expansion to make ChondroCelect.
3. An arthrotomy, during which a biodegradable cover is sutured over the cartilage defect under which the cultured cells are injected.

Following this intervention a rehabilitation programme is required.

Innovation and/or advantages

If licensed ChondroCelect will be the first advanced autologous chondrocyte therapy product developed for this indication.

Developer

TiGenix NV.

Availability, launch or marketing dates, and licensing plans:

In clinical trials.

NHS or Government priority area:

This topic is relevant to the National Service Framework: Long-Term Conditions (2005).

Relevant guidance

- NICE technology appraisal. Autologous chondrocyte implantation (ACI) for the treatment of cartilage injury (review of existing guidance TA16). 2005. (Guidance review deferred until 2012)¹.
- NICE guidance. Mosaicplasty for knee cartilage defects. 2006².
- NICE guidance. Mini-incision surgery for total knee replacement. 2005³.

Clinical need and burden of disease

Cartilage damage in the knee can be caused directly by injury, often as a result of sporting activity, or spontaneously (a condition called osteochondritis dissecans). Softening of the kneecap cartilage (a condition called chondromalacia patellae) may be caused by trauma, overuse, parts being out of alignment, or muscle weakness, and most often occurs in young adults. Loss of cartilage alone is referred to as chondral damage, whereas loss of bone and cartilage is known as osteochondral damage. Damaged articular cartilage fails

to heal on its own and can be associated with symptoms such as knee pain, knee swelling, knee locking and giving way of the knee joint. Ultimately, mechanical damage to the joint surface can lead to osteoarthritis¹.

The prevalence or incidence of cartilage damage in knee joints is not accurately known. NICE estimate that in the UK, 10,000 patients each year may suffer cartilage damage warranting repair¹. Of this total it is anticipated that approximately 9-12% could be treated with ChondroCelect (approximately 900-1200 patients per year)^a.

Existing comparators and treatments

There is no uniform approach to managing knee cartilage defects. Current treatment options used in sequence or combination include¹:

- Symptomatic relief.
- Procedures to re-establish the articular surface such as:
 - ACI
 - Marrow stimulation techniques - abrasion arthroplasty, drilling and microfracture.
 - Mosaicplasty - also known as osteochondral transplantation.
- Knee lavage with or without debridement.
- Knee replacement - for end stage knee joint failure caused by osteoarthritis.

Efficacy and safety

Trial code	NCT00414700: knee cartilage defects; ChondroCelect vs microfracture; phase III ^{4,5} .
Sponsor	TiGenix
Status	18-month data published, extension phase ongoing.
Location	Europe
Design	Randomised, controlled.
Participants in trial	n=118; adults; symptomatic knee cartilage defects of the femoral condyles; single grade III to IV. Randomised to CCI or microfracture. All patients followed the same rehabilitation programme.
Follow-up	12 months post-surgery.
Primary outcome	Efficacy; overall histology assessment score (ICRS II); knee osteoarthritis outcome score (KOOS); safety.
Secondary outcomes	VAS pain score.
Key results	CCI resulted in better structural regeneration (p=0.003) and overall histologic evaluation (p=0.012). Analysis of the tissue regeneration at 12 months indicated that CCI is associated with more chondrocyte-like cells and a higher proteoglycan content of the cellular matrix. Clinical outcome at 12-18 months: CCI was comparable with microfracture. Both treatment groups had similar mean baseline overall knee injury and osteoarthritis outcome score (56.30±13.61 and 59.53±14.95) for microfracture and CCI respectively, which increased in both groups to: 70.56±12.39 and 72.63±15.55 at 6 months; 73.26±14.66 and 73.10±16.01 at 12 months; and 74.73±17.01 and 75.04±14.50 at 18 months, respectively.
Expected reporting date	Study started in March 2002 and estimated completion date is December 2009.
Adverse effects	Both techniques were generally well tolerated. For the CCI and microfracture groups: arthralgia was the most commonly reported AE (61% vs 57% respectively); more

^a Information from the company.

	patients in the CCI group experienced joint swelling (19% vs 4.9% p=0.022), which occurred between 1-14 days after arthrotomy in CCI group.
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Estimated cost and cost impact

The cost of ChondroCelect has not been determined. A biodegradable cover (a periosteal flap or a collagen membrane) will be part of the CCI procedure and is estimated to cost £400-£500.

In 2005 the costs of arthroscopic and open knee ACI, microfracture and mosaicplasty were estimated in an HTA report⁶. These 2005 estimates were then adjusted by 12.05% in line with the Hospital and Community Health Services Pay and Prices Index to provide recent cost estimates of current treatment options^{7,b}:

Treatment	Estimated cost per treatment
Arthroscopic ACI and cell culture	£7,154
Open knee ACI and cell culture	£9,688
Microfracture	£2,631
Mosaicplasty	£4,157

Potential or intended impact – speculative

ChondroCelect would have a similar place in treatment as other ACI treatments currently performed on the NHS, though it may be a cheaper alternative^c.

Patients

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Reduced morbidity | <input type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Services

- | | | |
|--|--|--|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service reorganisation required | <input checked="" type="checkbox"/> Staff or training required |
| <input type="checkbox"/> Decreased use | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Costs

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input type="checkbox"/> New costs: | <input type="checkbox"/> Savings: | <input type="checkbox"/> Other: |

References

- ¹ National Institute of Health and Clinical Excellence. Autologous chondrocyte implantation (ACI) for the treatment of cartilage injury. Technology appraisal TA89 (review of existing guidance TA16). May 2005.
- ² Interventional Procedures Programme. Mosaicplasty for knee cartilage defects. Guidance IPG162. March 2006.
- ³ Interventional Procedures Programme. Mini-incision surgery for total knee replacement. Guidance IPG117. March 2005.
- ⁴ Clinical trials. Prospective multicenter randomised controlled trial of ChondroCelect (in an autologous chondrocyte transplantation procedure) vs microfracture in the repair of symptomatic defects of the knee. Available at: <http://clinicaltrials.gov/ct2/show/NCT00414700?term=ChondroCelect&rank=1> (accessed 15.8.08).

^b Information from the company.

^c Expert opinion.

- ⁵ Saris DB, Vanlauwe J, Victor J et al. Characterized chondrocyte implantation results in better structural repair when treating symptomatic cartilage defects of the knee in a randomized controlled trial versus microfracture. *American Journal of Sports Medicine*. 2008;36(2):235-46.
- ⁶ Clar C, Cummins E, McIntyre L et al. Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints: systematic review and economic evaluation. *Health Technology Assessment*. 2005;9(47):1-98.
- ⁷ Curtis L. Unit Costs for Health & Social Care. Personal Social Services Research Unit (PSSRU), University of Kent. 2007. Available at: <http://www.pssru.ac.uk/uc/uc2007contents.htm> (accessed 19.8.08).

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