ISRCTN98997175 https://doi.org/10.1186/ISRCTN98997175

Autologous Stem cells, Chondrocytes Or the Two?

Submission date	Recruitment status	[ ] Prospectively registered
10/05/2011	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
16/09/2013	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
31/03/2026	Musculoskeletal Diseases	[X] Record updated in last year

Plain English summary of protocol
Background and study aims
Osteoarthritis is a condition that affects the bone and cartilage (the protective surface that allows your joints to move smoothly). Symptoms include joint damage, pain and loss of mobility, and in the longer term most patients need a total joint replacement. Cell therapy is a novel method of treating patients with damaged cartilage and bone, but it is not yet known which type of cells would do this best. Patients with cartilage damage have been treated with cartilage cells (chondrocytes) for over 10 years and patients with bone fractures that fail to heal properly are treated with stem cells from their bone marrow. In all, over 400 patients to date have been treated with their own cells for cartilage and/or bone repair. These patients are treated with cells that have been grown in specialist facilities available on the hospital site from small samples of their own cartilage or bone marrow. Since this technique uses the patients' own cells (called autologous), the cells are not likely to cause an immune reaction. The aim of this study is to see whether stem cells from bone marrow will be able to repair the damage to joints better than cartilage cells, or if the two cell types are better when used in combination.

Who can participate?
Patients aged between 18 and 80 with osteoarthritis of the knee.

What does the study involve?
Participants will be randomly allocated to be treated with either stem cells from bone marrow, cartilage cells, or both cell types combined. All participants will be followed up for 20 years after treatment.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
Robert Jones and Agnes Hunt Orthopaedic Hospital (UK).

When is study starting and how long is it expected to run for?
September 2011 to September 2035.

Who is funding the study?
Arthritis Research UK.

Who is the main contact?
Dr Naomi Dugard, naomi.dugard@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Naomi Dugard

Contact details
Arthritis Research Centre
The Robert Jones and Agnes Hunt Orthopaedic Hospital
Oswestry
United Kingdom
SY10 7AG
+44 (0)1691 404139
naomi.dugard@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
2010-022072-31

Integrated Research Application System (IRAS)
50345

Protocol serial number
R5242 A789

Study information

Scientific Title
Autologous cell therapy for osteoarthritis: an evaluation of the safety and efficacy of autologous transplantation of articular chondrocytes and/or bone marrow-derived stromal cells to repair chondral/osteochondral lesions of the knee

Acronym
ASCOT

Study objectives
The ASCOT trial will be testing the following three alternative hypotheses:
1. Using autologous bone marrow stromal cells (BMSCs to repair chondral or osteochondral defects in the knee gives a different functional outcome from using autologous chondrocytes.
2. Using a combination of autologous BMSCs and autologous chondrocytes to repair chondral or

osteochondral cartilage defects in the knee gives a different outcome from using autologous chondrocytes alone.
3. Using a combination of autologous BMSCs and autologous chondrocytes to repair chondral or osteochondral cartilage defects in the knee gives a different outcome from using autologous BMSCs alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. NRES Committee West Midlands - Coventry & Warwickshire; 29/07/2011; Ref: 11/WM/0175
2. Substantial amendment (AM1 21/05/2013) approval date: 06/06/2013
3. Non-substantial amendment (AM2 19/06/2013) acknowledgement date: 16/09/2013
4. Substantial amendment (A3 09/12/2014) approval date 15/01/2015
5. Substantial amendment (A4 11/06/2018) approval date 12/07/2019
6. Non-substantial amendment (AM5 09/04/2020) acknowledgement date: 22/05/2020
7. Non-substantial amendment (AM6 11/12/2020) acknowledgement date: 17/12/2020
8. Substantial amendment (A7 05/05/2023) approval date 03/07/2023
9. Substantial amendment (A8 25/02/2025) approval date 11/03/2025

Study design
Single-centre single-blind three-arm randomised controlled trial with long-term follow-up

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Symptomatic cartilage defects in the knee

Interventions
According to the treatment allocation, trial participants will receive one of the three following cell therapy strategies:
1. Autologous chondrocytes:
1.1. One syringe containing resuspended autologous chondrocytes will be supplied, containing between 1 and 20 million cells depending on the cell kinetics of the individual patient
1.2. It is recommended that the full dose is used
2. Bone marrow-derived stromal cells (BMSCs):
2.1. One syringe containing resuspended autologous BMSCs will be supplied, containing between 1 and 20 million cells depending on the cell kinetics of the individual patient
2.2. It is recommended that the full dose is used
3. Autologous chondrocytes and BMSCs combined:
3.1. Two syringes will be supplied, one containing resuspended autologous chondrocytes and one containing resuspended BMSCs, each containing between 1 and 20 million cells, depending on the cell kinetics of the individual patient
3.2. It is recommended that half of each syringe will be used
3.3. Therefore the patient will receive a total cell population of between 1 and 20 million cells
3.4. This will prevent a bias of one group in the study having generally twice the number of cells in the other two groups

4. Each of the three groups will receive the intervention in two stages:
4.1. Cell harvesting stage
4.2. Cell implantation stage
5. There is approximately 3 weeks between the two stages
6. All participants will be followed up for 20 years after the second stage of treatment is complete

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Autologous articular chondrocytes and/or bone marrow-derived stromal cells

Primary outcome(s)
Patient-reported functional knee score (Modified Lysholm) at 15 months, taking into account the pre-operative score as a covariate

Key secondary outcome(s))
1. Incidence of adverse events
2. Quality of the repair tissue determined using the Oswestry Arthroscopy Score, for which participants will undergo a repeat arthroscopy between 12 and 15 months
3. A 2mm diameter needle biopsy will also be taken at this time, and the histology analysed by a blinded assessor using the International Cartilage Repair Society (ICRS) II histology scoring system
4. An MRI/CT scan will also be performed, with the participants' agreement, and scored by a blinded assessor using the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) Score
5. Health related quality of life, pain, knee function, activity levels and general mood of the patient will be assessed at 2m, 12m, 15m and annually up to 20 years post treatment using the following scores respectively:
5.1. The Veterans Rand 12 Item Health Survey (VR-12)
5.2. the Intermittent and Constant Osteoarthritis Pain score (ICOAP)
5.3. KOOS physical function short form (KOOS-PS)
5.4. Modified Lysholm Score
5.5. Human Activity Profile (HAP)
5.6. International Positive and Negative Affect Schedule Short Form (I-PANAS-SF)
6. Number of years free from further surgery
7. Observed patterns of rehabilitation and compliance to physiotherapy schedules will be collected using a participant diary up to 15 months post treatment
8. Unit costs per treatment will be recorded in order to perform a cost utility analysis

Completion date
01/09/2035

Eligibility

Key inclusion criteria

1. A symptomatic defect of the knee that extends to (Outerbridge grade 4) or into the subchondral bone
2. The patient will be aged between 18 and 80 years at the time of surgery
3. The defect is considered suitable for ACI
4. Surgical treatment has been performed on the same defect at least 6 months previously and has failed to relieve symptoms
5. The patient is able to provide written informed consent to participate in the trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Total final enrolment
114

Key exclusion criteria
1. English is not the first language of the patient
2. Likely to show contraindications to autologous cell therapy:
2.1. Osteoarthritis
2.2. Inflammatory arthritis
2.3. Previous or current malignant tumour
2.4. Therapy with steroids or methotrexate
2.5. Bleeding tendency or known anaphylaxis to any product used in chondrocyte preparation
3. Low probability of compliance with physiotherapy or follow-up, including a major life threatening condition
4. A defect of greater than 20cm2 in total area
5. The patient is shown to be positive for serology tests required by the cell provider. This includes:
5.1. HIV
5.2. Hepatitis B and C
5.3. Syphilis
5.4. Human T cell lymphotrophic virus (HTLV) I & II
6. Pregnancy or lactation
7. Exclusion criteria (5) and (6) will not be confirmed until after written informed consent is obtained

Date of first enrolment
01/09/2011

Date of final enrolment
01/10/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Robert Jones and Agnes Hunt Orthopaedic Hospital
Robert Jones and Agnes Hunt Orthopaedic Hospital
Twmpath Lane
Gobowen
Oswestry
England
SY10 7AG

Sponsor information

Organisation
Robert Jones and Agnes Hunt Orthopaedic Hospital (UK)

ROR
https://ror.org/030mbcp39

Funder(s)

Funder type
Charity

Funder Name
Arthritis Research UK ref: 18480

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No