ISRCTN14015902 https://doi.org/10.1186/ISRCTN14015902

Managing Avascular Necrosis Treatments: an Investigational Study (MANTIS)

Submission date
11/06/2018

Recruitment status
No longer recruiting

Registration date
12/06/2018

Overall study status
Completed

Last Edited
03/11/2022

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Avascular necrosis (AVN) is death of bone tissue due to interruption of the blood supply. The aim of this study is to assess the effect of a bisphosphonate drug treatment (Alendronate) on AVN of the hip.

Who can participate?
Patients aged 18 and over with AVN of the hip

What does the study involve?
Participants are randomly allocated to receive either a 12 month course of oral alendronate (70 mg taken weekly), or a matched placebo (dummy drug). This is in addition to standard care for the condition which includes non-weight bearing periods and over the counter pain medication. Participants are followed up for 3 years with follow-up assessments at 6, 12, 24 and 36 months and compliance assessments at 1, 2, 3, 6, 9 and 12 months: patients complete these assessments via questionnaires either in a paper format or through a secure online portal (the electronic data capture is planned to improve completion rates for the younger and more geographically mobile population). An x-ray is taken at 1 year and 3 years as part of standard routine care of patients with AVN, and the notes and images from these scans are collected. Those that haven't had any surgery also have an MRI scan at 3 years of which the images and notes are collected. The study includes a pilot study, which progresses to the definitive trial if predefined criteria regarding recruitment are met. In the initial pilot study, a minimum of 50 patients are randomly allocated over 12 months from at least 10 sites, with a target recruitment rate of 1-2 patients per site per month. AVN is an uncommon condition, therefore the aim of the pilot study is to maximise recruitment, and ensure that outcomes can be collected reliably and remotely in all patients. It will also provide information on site feasibility.

What are the possible benefits and risks of participating?
The results of this study will improve understanding of how Alendronate works which may help to improve the treatment for future patients with AVN. Alendronate is routinely used as osteoporosis treatment and therefore has a highly reviewed safety profile. As with any medication there are risks involved and recent evidence indicates the following side effects occurred in less than 10% of patients: headache, dizziness, vertigo, abdominal pain, indigestion,

constipation, diarrhoea, abdominal swelling, acid reflux, alopecia, itching, joint swelling, physical weakness or lack of energy and a build-up of fluid. Bone, muscle or joint pain is also a very common side effect occurring in more than 1 in 10 patients. There is limited information available regarding the effect of alendronate on pregnancy therefore highly effective contraceptive methods are required for all participants (regardless of sex or gender) for the duration of the study treatment and for a year after completing the treatment.

Where is the study run from?
Nuffield Orthopaedic Centre (UK)

When is the study starting and how long is it expected to run for?
June 2017 to December 2022

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Miss Gemma Greenall
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Study website
https://www.ndorms.ox.ac.uk/clinical-trials/current-trials-and-studies/m

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2017-002798-21

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
37920

Study information

Scientific Title
A multi-centre, blinded, randomised, placebo-controlled trial assessing the clinical and cost effectiveness of a 12 month course of oral alendronate (70 mg weekly) in patients presenting with avascular necrosis of the hip - Managing Avascular Necrosis Treatments: an Interventional Study (MANTIS)

Acronym
MANTIS

Study objectives
To assess the effect of bisphosphonate treatment (alendronate) on avascular necrosis (AVN) of the hip.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Oxford A Research Ethics Committee, 29/05/2018, ref: 18/SC/0247

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Avascular necrosis of the hip

Interventions
Randomisation will be performed using a minimisation algorithm including random elements to ensure balanced allocation of participants across the two treatment groups stratified by:
1. Randomising site

2. FICAT stage (1 or 2)
3. Main AVN risk factors (steroid/alcohol/other) obtained from clinical notes
4. Bilateral vs unilateral AVN

Patients will be randomised on a 1:1 basis to receive either a 12 month course of oral alendronate (one 70mg tablet taken weekly), or a matched placebo. This will be in addition to standard care for the condition which includes non-weight bearing periods and over the counter pain medication.

Patients, clinicians and assessors will be blinded to the treatment allocation. Patients will be followed up for 3 years with follow up assessments at 6, 12, 24 and 36 months and compliance assessments at 1, 2, 3, 6, 9 and 12 months: patients will complete these assessments via questionnaires either in a paper format or through a secure online portal (the electronic data capture is planned to improve completion rates for the younger and more geographically mobile population).

An x-ray will be collected at 1 year and 3 years as part of standard routine care of patients with AVN, and the notes and images from these scans will be collected. Those that haven't had any surgery will also have an MRI scan at 3 years of which the images and notes will be collected.

The study will include a pilot study, which will progress to the definitive trial if predefined criteria regarding recruitment are met. In the initial pilot study, a minimum of 50 patients will be randomised over 12 months from at least 10 sites, with a target recruitment rate of 1-2 patients per site per month. AVN is an uncommon condition, therefore the aim of the pilot study is to maximise recruitment, and ensure that outcomes can be collected reliably and remotely in all patients. It will also provide information on site feasibility.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Alendronate

Primary outcome measure
Hip function measured using Oxford Hip Score (OHS) at 12 months

Secondary outcome measures
1. Hip function and quality of life (QoL) measured using Oxford Hip Score (OHS), iHOT-33, Hospital Anxiety and Depression Score (HADS) and EQ-5D-5L at baseline, 6, 12, 24 and 36 months
2. Radiological progression measured using x-ray at 12 and 36 months and MRI at 36 months
3. Treatment compliance measured using bespoke compliance questionnaires at 1, 2, 3, 6, 9, and 12 months
4. Cost effectiveness measured using healthcare resource use questionnaires at 6, 12, 24 and 36 months

Overall study start date
01/06/2017

Completion date
31/08/2020

Eligibility

Key inclusion criteria
1. Early, symptomatic, atraumatic AVN of the hip (Ficat score 1 or 2 using MRI)
2. Aged 18 years or over

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 280; UK Sample Size: 280

Total final enrolment
21

Key exclusion criteria
1. Diagnosis not confirmed their diagnosis (Ficat 1 or 2), using MRI, within the last 12 months
2. Renal function (creatinine clearance) of < 30 ml/min (tested within the last 3 months)
3. Adjusted serum calcium levels outside local reference range (tested within the last 3 months)
4. Established osteoarthritis (Kellgren-Lawrence >=2)
5. Previous AVN, femoral head deformity, prior hip surgery or hip fracture in the index hip
6. Current pathology (e.g. osteoporosis) that requires treatment with bisphosphonates
7. Received previous anti-osteoporosis therapy (excluding calcium or vitamin D supplements) that lasted more than 4 weeks for oral treatment or any length of parenteral treatment
8. Contraindications to MRI
9. Contraindications to alendronate therapy (including hypocalcaemia) as listed in the SmPC
10. Planning a pregnancy in the next 12 months or are currently pregnant or breastfeeding
11. Not using appropriate contraception and of child bearing age
12. Have a planned joint preserving surgical procedure of the hip
13. Unable to provide informed consent
14. Unable to commit to follow-up regime
15. Already enrolled in an interventional clinical trial

Date of first enrolment
15/07/2018

Date of final enrolment
17/11/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nuffield Orthopaedic Centre (lead site)
Windmill Road
Headington
Oxford
United Kingdom
OX3 7HE

Sponsor information

Organisation
University of Oxford

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type

Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 15/39/06

Results and Publications

Publication and dissemination plan
Results of this trial will be submitted for publication in a peerreviewed journal. All presentations and publications will be preagreed by the Trial Steering Committee (TSC).

Intention to publish date
01/08/2021

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/10/2022	03/11/2022	Yes	No
HRA research summary			28/06/2023	No	No