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Pain Reduction in Osteoarthritis of the knee using oral Methotrexate

Submission date	Recruitment status	[ ] Prospectively registered
08/12/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
09/05/2011	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/06/2013	Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
RR08/8797

Study information

Scientific Title
An open label study to assess the effectiveness of oral methotrexate at reducing pain in knee osteoarthritis

Acronym

PROM

Study objectives
Osteoarthritis (OA) is the most common arthritis worldwide and causes significant pain and disability. Current treatments including non-steroidal anti-inflammatory drugs (NSAIDs) and opioids have significant side-effects. There is an urgent need for safe, long-term treatments for pain in OA.

Recent imaging studies, in particular magnetic resonance imaging (MRI) have demonstrated that synovitis is very common in OA of the knee and strongly associated with pain. Methotrexate (MTX) is a safe and effective treatment for synovitis with good efficacy and long-term safety in inflammatory arthritides. This 24 week open label study evaluates the effectiveness of methotrexate at pain reduction in knee OA. We also assessed ultrasound-detected synovitis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds (West) Research Ethics Committee approved on the 26th March 2009 (ref: 09/H1307/11)

Study design
Single centre open label study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Osteoarthritis of the knee

Interventions
Oral methotrexate up to 20 mg for 24 weeks. No placebo (open label).

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
Change in VAS (0 - 100 mm) pain scores at 24 weeks. VAS pain scores will be measured at baseline and 24 weeks, to assess knee pain within the last 48 hours.

Key secondary outcome(s))
1. Changes on ultrasound scan at baseline and 24 weeks. Ultrasound images will be scored for synovitis and effusion, measured in milimetres.

2. Change in Osteoarthritis Quality of Life Questionnaire (OAQoL) score, measured at baseline, 12 and 24 weeks
3. Change in Hospital Anxiety and Depression Scale (HADS) score, measured at baseline, 12 and 24 weeks
4. Change in Western Ontario and McMasters University Index (WOMAC) pain, function and stiffness subscales , measured at baseline, 12 and 24 weeks
5. Change in West Haven-Yale Multidimensional Pain Inventory scores, measured at baseline, 12 and 24 weeks
6. Change in VAS pain scores measured at baseline and 12 weeks

Completion date
31/03/2011

Eligibility

Key inclusion criteria
1. Knee pain on most days in the last 3 months
2. Insufficient pain relief from, or inability to tolerate NSAIDs and/or opioids
3. Patient able to identify a predominantly painful knee (the signal knee)
4. Moderate to severe pain of the signal knee as defined by a score of greater than or equal to 40 mm on a Visual Analogue Scale (VAS) (0 - 100 mm) using the question "On average, how would you rate your knee pain during the last 3 months?"
5. Fulfil clinical American College of Rheumatology (ACR) criteria for knee OA
6. A previous radiograph (X-Ray) of the signal knee with changes consistent with osteoarthritis
7. Men and women must use adequate birth control measures (e.g. abstinence, oral contraceptives, intra-uterine device, barrier method with spermicide, or surgical sterilisation) for the duration of the study and should continue such precautions for 6 months after receiving the last dose of methotrexate. If female and have potential for child bearing then a negative pregnancy test must be performed prior to starting treatment.
8. The patient must be able to adhere to the study visit schedule and other protocol requirements
9. The patient must be capable of giving informed consent and the consent must be obtained prior to any screening procedures
10. All patients with pre-existing lung disease/smokers must have had a chest radiograph (X-Ray) within the last 6 months
11. Aged 53 - 85 years, either sex

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria

1. The presence of any rheumatic diseases that could be responsible for secondary osteoarthritis
2. Use of intra-articular hyaluronic acid in the signal knee or the use of depo corticosteroid injection within the 6 months preceding enrolment in the study
3. Use of intra-articular corticosteroid injections in the 3 months preceding enrolment
4. The use of oral or parenteral steroids in the 2 months preceding the study
5. Knee injury or diagnostic arthroscopy within the 6 months preceding enrolment in the study
6. A history of knee surgery in the signal knee at any time
7. The presence of non-OA causes of pain in the signal knee, e.g. referred hip pain, osteonecrosis
8. Women who are pregnant, nursing, or men or women planning pregnancy within 12 months after screening (i.e. approximately 6 months following last study medications)
9. Use of any investigational (unlicensed) drug within 1 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer
10. Significant haematological or biochemical abnormality:
10.1. Haemoglobin less than or equal to 8.5 g/dL
10.2. White cell count (WCC) less than or equal to 3.5 x 109/L
10.3. Neutrophils less than or equal to 1.5 x 109/L
10.4. Platelets less than or equal to 100 x 109/L
10.5. Alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) for the laboratory conducting the test
10.6. Creatinine greater than 1.5 times ULN for the laboratory conducting the test
11. Have current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, haematological, gastrointestinal, endocrine, pulmonary, cardiac, neurologic, or cerebral disease
12. Intake of alcohol above the recommended government guidelines (2 units per day for women, 3 units per day for men)
13. Poor tolerability of venepuncture or lack of adequate venous access for required blood sampling during the study period

Date of first enrolment
31/07/2009

Date of final enrolment
31/03/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Section of Musculoskeletal Disease
Leeds
United Kingdom
LS7 4SA

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
University/education

Funder Name
University of Leeds (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

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?
Results article	results	01/05/2013		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes