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Effects of intra-articular administration of Hymovis on the expression and activity of matrix metalloproteinases in synovial fluids of patients affected by osteoarthritis of the knee

Submission date
01/08/2014

Recruitment status
No longer recruiting

Registration date
15/09/2014

Overall study status
Completed

Last Edited
15/10/2020

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Osteoarthritis (OA) is a degenerative disease of the joint. Over time, the cartilage covering the end of the bones at the joints become rough and thin, and in some cases wearing out completely, so that the bones in the joint grind against each other. Symptoms include painful and stiff joints and a limited range of movement. It can have a serious impact on the life of the individual with the condition as well as on public health services. Matrix metalloproteinase 3 (MMP3) is an enzyme known to be involved in the breakdown of cartilage and it can be found in the joint fluid (synovial fluid) of patients suffering from OA of the knee. Here, we want to see if injecting the knee with a synovial fluid replacement, Hymovis (a hyaluronic acid), can reduce the amount of MMP3 present and relieve pain. Hymovis has already been shown to work in the laboratory. We also hope to see whether Hymovis can also have an effect on other proteins that may be involved in OA.

Who can participate
Adults aged at least 46 with OA of the knee.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are treated with Hymovis. Those in group 2 are treated with another hyaluronic acid called Synvisc. Both groups are given 3 injections in all. The synovial fluid in the knee is collected and analysed before the first and second injection to check for MMPs and other molecules that suggest that there is inflammation. All patients are followed up for 6 months. At the end of the study, we assess the performance of the two treatments.

What are the possible benefits and risks of participating?
There are no immediate direct benefit for those taking part in this study, but there should be benefits for future patients. It is possible that the treatment will relieve knee OA pain. The main risks are pain, swelling or infections.

Where is the study run from?
This study has been set up by Fidia farmaceutici S.p.A. and it will be carried out by the Medicine Department of the University of Perugia (Italy)

When is the study starting and how long it is expected to run for?
September 2014 to September 2015

Who is funding the study?
Fidia farmaceutici S.p.A. (Italy)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EQC5-14-01

Study information

Scientific Title
A post-marketing, pilot study to assess the role of intra-articular administration on the expression and activation of metalloproteinases in synovial fluid.

Study objectives

It is hypothesized that Hymovis has the capacity to decrease the expression ad activation of MMPs in synovial fluid, the purpose of the study is to verify this activity comparing it to that of another product for the same indication

Ethics approval required
Old ethics approval format

Ethics approval(s)
Umbria Ethic Committee (CEAP), 21/05/2014, ref. CEAS N 2333/14

Study design
Pilot study, randomized open label post marketing

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Knee Osteoarthritis

Interventions
Patients are randomly allocated into one of two groups. One group is treated with Hymovis hyaluronic acid (HA) and the other group, Synvisc HA.
All patients will undergo one cycle of intra-articular injections with HA, synovial fluid will be collected at baseline and before the second injection. 6 visits are scheduled:
Screening visit: enrolment
Visit 1: Start of therapy (first injection)
Visit 2: During study treatment (second injection)
Visit 3: During study treatment (third injection)
Visit 4: First FU (3 months after baseline)
Visit 5: Second FU (6 months after baseline)

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure

1. Synovial fluid analysis will be carried out at baseline and at visit 1
2. MMP3 activity will be evaluated via ELISA test

Secondary outcome measures
The following variables will be evaluated at baseline and visit 1:
1. Macroscopic analysis of SF
2. Microscopic analysis of SF
3. Expression of MMP2 and MMP13 (ELISA test)
4. Expression of inflammatory cytokines (Flowcytomix analysis)
At baseline and FU visits the following will be considered:
1. VAS
2. WOMAC
3. Physicians global assessment
For all the duration of the study safety and tolerability will be assessed by recording all AE

Overall study start date
03/09/2014

Completion date
03/09/2015

Eligibility

Key inclusion criteria
1. Ambulant patient > 45 years of age in good health conditions
2. Patient of any race, both outpatients or hospitalized, affected by OA diagnosed both clinically and radiologically according to the American College of Rheumatology criteria:
2.1. Pain
2.2. Presence of radiographic osteophytes
2.3. At least one of the following items:
2.3.1. Age > 50
2.3.2. Morning stiffness < 30 minutes of duration
2.3.3. Crepitus on motion
3. Kellgren-Lawrence grade II-IV confirmed by X-ray (performed within 6 months preceding the inclusion in the study)
4. Patient diagnosed with idiopathic OA of the knee since at least one year
5. Patient presenting synovial effusion of the knee joint echographically confirmed
6. Patient who discontinued previous oral/topic NDAIDs therapy since at least one week before the first intra-articular injection
7. Male or fertile, non pregnant or breast feeding female who consents to use a reliable birth control method for the whole treatment duration
8. Patient without conditions or psychological impairment who could interfere with compliance to the protocol and the study conclusion in the investigator's opinion
9. Patient able to understand study obligations and who provided a written informed consent in compliance with the Helsinki declaration (version October 2013)

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
30

Key exclusion criteria
1. Concomitant chronic inflammatory diseases (e.g. rheumatoid arthritis or psoriasis)
2. Painful knee condition other than OA
3. Secondary knee OA or relevant knee injuries in the target knee within 6 months before the inclusion
4. Known or suspected allergic reactions to hyaluronic preparations or to other components of the devices under study
5. Presence of infections and/or skin diseases in the area of injection site; e.g. psoriasis
6. Known coagulopathy
7. Therapy with one of the devices under study within 6 months before the inclusion
8. Systemic anti-inflammatory therapy at a fixed dose within 1 month before the inclusion
9. In therapy with i.a. HA or i.a. corticosteroids within 6 months before the inclusion
10. In therapy with biphosphonates, and/or oral pharmaceutical products containing glucosamine and/or chondroitin sulphate and/or diacerein within 1 month before inclusion
11. Participation in any other study involving investigational or marketed products simultaneously or within one month prior to study entry
12. Previous surgery in the target knee within 9 months prior to inclusion, or planned surgery throughout the duration of the study
13. Presence of pathologies or conditions that might interfere with subject compliance /cooperation during the study, in the judgment of the investigator
14. History of alcoholism, treatment abuse, psychological or other emotional problems that, in the judgment of the investigator, could invalidate informed consent or limit the subjects compliance with protocol requirements
15. Females who are pregnant, lactating or not in menopause and are not using recognized contraceptive measures as indicated by investigators for the duration of the study

Date of first enrolment
03/09/2014

Date of final enrolment
03/09/2015

Locations

Countries of recruitment
Italy

Study participating centre

Università degli Studi di Perugia
Perugia
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Sponsor information

Organisation
Fidia Pharmaceuticals S.p.a (Fidia Farmaceutici S.p.a) (Italy)

Sponsor details
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Sponsor type
Industry

ROR
https://ror.org/00stv9r10

Funder(s)

Funder type
University/education

Funder Name
University of Perugia (Italy)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration