Hydros Joint Therapy and Hydros TA for Pain Associated with Knee Osteoarthritis; A Prospective, Multi-center, Randomized, Double-blind Feasibility Study to Evaluate the Safety and Performance of Hydros Joint Therapy and Hydros TA for Management of Pain Associated with Osteoarthritis in the Knee

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The purpose of this study is to evaluate the safety and performance of Hydros and Hydros with triamcinolone acetonide, (Hydros TA) for treatment of pain from osteoarthritis of the knee, in patients who have failed to respond adequately to...

Ethical review	-
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON34625

Source
ToetsingOnline

Brief title
COR 1.0

Condition

- Joint disorders

Synonym
Joint damage, joint degeration

Research involving
Human

Sponsors and support

Primary sponsor: Carbylan BioSurgery, Inc.
Source(s) of monetary or material Support: Industrie: Carbylan BioSurgery;Inc.

Intervention

Keyword: Hyaluron, Hydros Joint Therapy, Osteoarthritis, Synvisc One

Outcome measures

Primary outcome

Primary Endpoints

Effectiveness

WOMAC Pain Subscale Score

The WOMAC Pain Subscale is used to assess the severity of the knee pain at

Screening, Week 2 Follow-up, Week 6 Follow-up, Week 13 Follow-up, and Week 26

Follow-up visits. For each subject the scores of the five questions that

comprise the WOMAC Pain subscale are averaged.

The primary endpoint is the time-weighted change from baseline in the WOMAC

Pain sub-scale average score in the treatment knee.

Secondary analyses include the change from baseline to week 13 and change from

baseline to week 26.

Safety

The safety and tolerability of Hydros and Hydros TA will be evaluated by comparison of Adverse Event (AE) rates. AEs will be followed through resolution or 30 days after the subject terminates from the study, whichever occurs first.

Secondary outcome

Secondary Endpoints

Positive Responders

The number and percentage of subjects who have a positive response based on the OMERACT-OARSI set of responder criteria will be used to assess differences between the treatment groups in response to treatment for symptomatic primary OA of the knee over 26 weeks.

Paracetamol Usage

To assess differences in the amount of pain medication required over the treatment period, the average daily dosage of paracetamol (grams) will be assessed.

WOMAC Function Subscale Score

The WOMAC Function Subscale is used to assess the severity of the knee function at Screening, Week 2 Follow-up, Week 6 Follow-up, Week 13 Follow-up, and Week 26 Follow-up visits. For each subject the scores of the five questions that

comprise the WOMAC Function subscale are averaged.

WOMAC Stiffness Subscale Score

The WOMAC Stiffness Subscale is used to assess the severity of the knee function at Screening, Week 2 Follow-up, Week 6 Follow-up, Week 13 Follow-up, and Week 26 Follow-up visits. For each subject the scores of the five questions that comprise the WOMAC Stiffness subscale are averaged.

Study description

Background summary

Osteoarthritis (OA) is a common degenerative joint disease with 22 million men and women in the European Union affected1. About 6% of the European population age 30 and over have frequent knee pain and radiographic osteoarthritis. These findings are comparable to studies which estimate that 21 million women and men in the US who are 25 years and older (approximately 12.1%) are affected by OA and more than 40% of all adults over 75 years old are affected. OA is the leading cause of disability in Europe, the USA and Japan. Pain from osteoarthritis has a major influence on a patient*s quality of life and carries a heavy economic burden.

Osteoarthritis is characterized by loss of articular cartilage, subchondral bone sclerosis, osteophyte formation, changes in the synovial membrane, and reduced viscosity of synovial fluid.

There are limited options for treating pain associated with osteoarthritis. Treatments range from measures that limit weight impact on the joints, to oral analgesics and anti-inflammatory drugs, to steroid and viscosupplement intra-articular (IA) injections, and surgical joint replacement. The European League Against Rheumatism (EULAR) concludes that there is evidence to support the efficacy of hyaluronan (viscosupplements) in knee OA, for pain reduction and functional improvement, with greater length of time benefit than intra-articular steroids. As such, hyaluronan is an effective IA viscosupplementation therapy that is used to minimize pain and to facilitate joint movement in patients with OA of the knee.

Hyaluronan is a naturally occurring constituent of the extracellular matrix of

body tissues and is found in significant concentration in the synovial fluid and articular cartilage of joints. Hyaluronan functions by lubricating joints and by aiding articular mobility, thereby reducing pain. Various hyaluronan based products for intra-articular injection are now available and are used commonly worldwide to treat OA of the knee.

Clinical trials for the treatment of knee OA with intra-articular hyaluronan injection have been extensively analyzed and compared for their design and outcomes. A systematic review of six meta-analyses of hyaluronan in osteoarthritis of the knee show conflicting estimates of therapeutic effect; however, in the balance between benefit to harm, the probable benefit of pain reduction and physical function improvement outweighs the low risk of harm.

A meta-analysis of the literature on intra-articular corticosteroid injection for OA of the knee extracted ten randomised and controlled trials from a search of the Cochrane controlled trials register, Medline (1966 to 2003), and Embase (1980 to 2003). This meta-analysis concluded that the evidence supports short term (up to two weeks) improvement in symptoms of osteoarthritis of the knee after intra-articular corticosteroid injection. Raynauld et al. studied the safety of long-term (up to 2 years) intra-articular injection treatment with triamcinolone acetonide (40mg) in OA of the knee. The study concluded that with repeat intra-articular injections of triamcinolone acetonide every 3 months there were no deleterious effects on the anatomical structures of the knee, as measured by loss of joint space, at the one and two year follow-up evaluations. Moreover long-term treatment of knee OA with repeated steroid injections appears to be clinically effective for the relief of symptoms of the disease.

Studies have also evaluated the concomitant use of hyaluronan with steroids, anti-inflammatory drugs, and analgesic agents in an attempt to magnify the extent and duration of pain relief. In a one year study of hyaluronan with and without triamcinolone acetonide, both groups improved with the combination-therapy subjects improving sooner. Other clinical studies have successfully used steroids with hyaluronan for pain relief and consider this combination treatment as complementary therapy.

Future studies of hyaluronan combined with steroid treatment will add to the body of knowledge for management of OA of the knee. The Hydros product combined with TA to be evaluated here has distinct potential advantages from a safety and effectiveness standpoint.

Study objective

The purpose of this study is to evaluate the safety and performance of Hydros and Hydros with triamcinolone acetonide, (Hydros TA) for treatment of pain from osteoarthritis of the knee, in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g.,

paracetamol (acetaminophen). A three arm study will compare Hydros and Hydros TA, both investigational viscosupplements, to Synvisc-One, a commercially available viscosupplement. Viscosupplementation is a therapeutic technique that directly addresses the cause of pain, by replacing the low elastoviscous osteoarthritic synovial fluid with high elastoviscous solutions of hyaluronan or its derivatives. Triamcinolone acetonide, the steroid in Hydros TA, has been a standard therapeutic treatment for OA joint pain for over 40 years.

Study design

Study Design
This study is a multi-center, controlled, randomized, double blind study. All of the subjects will receive either Hydros, Hydros TA, or Synvisc-One injected into one treatment knee joint. Hydros and Hydros TA are investigational products (not approved for sale). The steroid component of Hydros TA (triamcinolone acetonide) and Synvisc-One are approved products for joint injection to treat pain related to osteoarthritis.
There will be four follow-up visits which will occur at 2 weeks, 6 weeks, 13 weeks, and 26 weeks after the injection. The procedures for the study are explained in detail in this document.

Intervention

Hydros is an absorbable gel made of a naturally occurring substance (hyaluronic acid). Hyaluronic acid (HA) is found in various tissues throughout the human body, including the natural fluid in the knee. The HA raw material used to manufacture Hydros is produced biosynthetically and contains no animal or human components. The product is supplied as a single injection, ready to use, in a 10 mL glass syringe containing 6 mL of sterile Hydros at physiologic pH.

Hydros TA is an absorbable gel made of a naturally occurring substance (hyaluronic acid), combined with a low dose, well-known steroid (anti-inflammatory drug), triamcinolone acetonide (TA). Triamcinolone acetonide is approved for injection into the knee joint to treat pain related to osteoarthritis. Hydros TA is supplied as a single injection, ready to use, in a 10 mL glass syringe containing 6 mL of sterile Hydros TA at physiologic pH.

Control material:

Synvisc-One (hylan G-F 20) is an elastoviscous high molecular weight fluid containing hylan A and hylan B polymers produced from chicken combs. Hylans are derivatives of hyaluronan (sodium hyaluronate). Hylan G-F 20 is unique in that the hyaluronan is chemically crosslinked. The contents of the syringe are sterile and non-pyrogenic. Synvisc-One is a single injection product that is approved for use in Europe and the USA.

Study burden and risks

As with all medical procedures, there are risks involved. You may experience side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don*t know all the side effects that may happen. Side effects may be mild or very serious. In rare cases side effects can be serious and long lasting. Your doctor will discuss the risks of this treatment with you.
The potential risks associated with the use of Hydros, Hydros TA and Synvisc-One may include those events that have been reported in association with other similar hyaluronan products. These risks include, but are not limited to, the following: pain, swelling and/or effusion in the injected knee, rash, hives, itching, fever, nausea, headache, dizziness, chills, muscle cramps, paresthesia (numbness, tingling), peripheral edema (swelling in the feet and legs).

Risks to subjects in this study may also include all the risks currently associated with corticosteroid therapy, which includes conditions that affect the following systems; fluid and electrolyte balance, musculoskeletal, cardiovascular, neurologic, gastrointestinal, dermatologic, endocrine, ophthalmic, metabolic and other areas.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Osteoarthritis (OA) grade 2 or 3 in one knee using Kellgren-Lawrence Grading for OA radiologically and verified within the prior 6 months.
a. Grade 2 defined as definite osteophytes with unimpaired joint space
b. Grade 3 defined as definite osteophytes with moderate joint space narrowing
2. Treatment knee criteria:
a. WOMAC Pain subscale score of 50-90 mm on a Visual Analogue Scale (VAS) (where 0 <= no pain and 100 mm <= worst pain) for the average of the five pain questions, and
b. One WOMAC Pain subscale score allowed to be below 20 mm or above 90 mm on the VAS.
3. Non-treatment knee WOMAC Pain subscale score less than or equal to 30 mm average of the five pain questions.
4. Symptoms in the treatment knee for at least 12 months.
5. Fully ambulatory subject (ability to perform a 15 meters walk test).
6. Male and female subjects 40 through 85 years of age.
7. Willing to NOT take any pain medication for 48 hours prior to each study visit and provide a list of pain medications taken between visits.
NOTE: Subject may take the following during the study:
a. Up to a maximum of 4 gm. paracetamol (acetaminophen) daily for treatment knee pain.
b. Single daily low dose ASA up to 325 mg.
c. Short term (3 days or less) NSAIDs for pain of origin other than treatment knee.
8. Written consent to participate in the clinical study following subject*s review of the COR 1.0 Study Subject Information and Consent form.
9. Able to understand the requirements of the study and willing to comply with all treatment and study evaluations for the duration of the trial.
10. Females of childbearing potential must not be or become pregnant for the duration of the study.

Exclusion criteria

1. Non-treatment knee joint pain greater than 30 mm average WOMAC Pain subscale scores.
2. Secondary OA resulting from rheumatoid arthritis, chondrocalcinosis, osteonecrosis, chronic fibromyalgia or other autoimmune disease.
3. Generalized symptomatic OA in lower extremity joints other than the knees, inflammatory joint disease, bursitis, OA in the hips, or other condition that may interfere with study assessments. Diagnosis is from medical history or prior xrays. Upper extremity OA is NOT excluded.

4. Active infection in either knee joint or adjacent tissues or positive synovial fluid culture of any joint.
5. Any contraindications for intra-articular injection or aspiration.
6. Knee surgery or trauma within 3 months prior to enrollment or planned joint surgery for the period of study duration.
7. Intra-articular steroid injection in the knee and/or use of systemic (oral) corticosteroids within 3 months prior to enrollment. Inhaled steroids are NOT excluded.
8. Intra-articular hyaluronan injection in the treatment knee within 6 months prior to enrollment.
9. BMI greater than 35.
10. Known hypersensitivity/allergic/anaphylactic reactions to local anesthetics.
11. Known sensitivity to avian proteins, corticosteroids, or hyaluronan-based products.
12. Arthroscopy of either knee or in any other joint within one (1) month prior to enrollment.
13. Started the use of glucosamine, chondroitin sulfate, diacerhein, or avocado/soya extracts within 2 months prior to Screening.
14. Current treatment with systemic steroids, narcotic analgesics, acetylsalicylic acid (ASA) greater than 325 mg daily, NSAIDs, COX inhibitors, or joint creams (e.g. methylsalicylate or capsaicin).
NOTE: Subject may take the following during the study:
a. Up to a maximum of 4 gm. paracetamol daily for treatment knee pain.
b. Single daily low dose ASA up to 325 mg.
c. Short term (3 days or less) NSAIDs for pain of origin other than treatment knee.
15. Current uncontrolled diabetes mellitus.
16. Current use of intra-articular injections.
17. Clinically significant conditions that would interfere with accuracy of study evaluations, e.g. malignant neoplastic disease, intra-articular tumor, fibromyalgia, peripheral neuropathy, vascular insufficiency, hemiparesis, significant psychiatric or neurological disorders, active alcohol/drug abuse, or other factors that the investigator feels would interfere with study evaluations and study participation.
18. Participation in another clinical trial and/or treatment received with any investigational agent within 30 days before enrollment

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-10-2010
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Intra-articular injection of Hydros Joint Therapy / Hydros TA Joint Therapy / Synvisc One
Registration:	No

Ethics review

Not available

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL30855.018.10

Study results

Date completed:	30-06-2011
Actual enrolment:	12

Summary results
Trial is onging in other countries