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

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

Summary

ID

NL-OMON40374

Source
ToetsingOnline

Brief title
COR 1.1

Condition

- Joint disorders

Synonym
Joint Degeneration, Osteoarthritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Hyaluron, Hydros Joint Therapy, Knee Pain Management, Osteoarthritis

Outcome measures

Primary outcome

The primary objective of the study is to evaluate Hydros-TA treated Subjects for the reduction of OA symptoms, compared to Hydros at 2 weeks and Hydros-TA compared to TA 10 mg at 26 weeks, as assessed by the WOMAC OA Index.

Secondary outcome

Secondary objectives will include a strict OMERACT-OARSI responder rate, time of onset of pain relief, time to treatment failure, change from baseline in WOMAC A (Pain), B (Stiffness) and C (Function), change from baseline in physician and subject global assessment scores at each follow-up visit, and a rescue medication use.

The safety of Hydros-TA will be evaluated by the assessment of all adverse events and through physical examinations.

Study description

Background summary

The sponsor conducted a prospective, multicenter, randomized, double-blind clinical trial (COR1.0) to compare the concomitant use of HA and steroid with currently available treatment options. The results demonstrated the potential benefits of concomitant use, benefits that are not available with current treatment options.

A single injection of Hydros or Hydros-TA was found to be well-tolerated and relieved pain associated with knee OA over 26 weeks. Hydros-TA showed a trend towards a faster onset of pain relief compared to the non-steroid containing products evaluated in the study. The results from the COR 1.0 study, in addition to results from nonclinical work, have provided evidence supporting the safety of Hydros-TA. These results support further development of Hydros-TA as a product that provides a combination of fast onset and sustained relief for the pain associated with osteoarthritis of the knee in a single injection. This dual action is not available with currently marketed treatments.

Study objective

The purpose of this study is to evaluate the safety and efficacy of Hydros-TA Joint Therapy for relief of pain due to OA of the knee. Hydros-TA is designed to provide fast acting and long lasting pain relief for up to six months with a single IA injection.

Study design

This is a multi-center, randomized, double-blind trial to be conducted at 30-40 centers in Canada, Europe, Australia, New Zealand and the Caribbean. Subjects who provide written informed consent, meet inclusion, and do not meet exclusion criteria will be enrolled, randomized, do not meet /exclusion criteria will be enrolled, randomized, criteria will be enrolled, randomized, treated, and followed for 26 weeks or 52 weeks
if the subject agrees to participate in an optional visit at 52 weeks post-treatment. A maximum of 510 Subjects (170/arm) will be randomized 1:1:1: to three treatment arms; Hydros-TA, TA 10mg and Hydros.

Intervention

Subjects will be treated with one 6mL intra-articular injection with either Hydros, Hydros-TA or Triamcinolone acetonide (10mg)

Hydros is a 6mL intra-articular injectable comprised of a bioresorbable hyaluronan-based hydrogel suspended in a hyaluronan solution.

Hydros-TA Joint Therapy is a 6mL intra-articular injectable comprised of 10mg triamcinolone acetonide encapsulated in hyaluronan-based hydrogel and suspended

in a hyaluronan solution.

Triamcinolone Acetonide is a well-known synthetic corticosteroid, approved for IA injections and is indicated as adjunctive therapy for short-term administration for acute episodes or exacerbations of OA. This study uses the commercially available product Kenalog-10 as comparator.

Study burden and risks

As with all medical procedures, there are risks involved. It is assumed that the discomforts that could manifest in this study are comparable to the symptoms potentially associated with known knee injections. Everyone taking part in the study will be watched carefully for any side effects. The investigator will discuss the risks of this treatment with the subjects.

Potential risks associated with the use of Hydros-TA may include the risks that have been reported in association with the use of other viscosupplements and with the use of IA TA.

The risks associated with the use of IA injection of similar HA products include, but are not limited to: Arthralgia (knee joint pain), Back pain, Effusion of the knee joint (increased fluid within the joint), Gastrointestinal symptoms (intestinal upset), Headache, Pain at injection site, Pain, stiffness or swelling in (injected) knee joint, Nasopharyngitis, Muscle spasms, Meniscal lesions, Arthropathy (knee joint disease) or arthrosis (joint condition related to nutrition), Knee joint stiffness or disorder, Asthenia (weakness), Baker*s cyst (closed sac inside joint), Bursitis (irritation of padding in joint), Dizziness, Edema in lower limb (swelling of leg, ankle), Erythema (warm, red, tender), edema (swelling), bruising, or rash at injection site, Facial swelling/flushing, Fatigue (tiredness), Fever, chills, Hives, rash (nonspecific area), Hypokinesia of knee (decreased motor reaction) Infection, Increase blood pressure, Immune response (inflammation and/or cell reactions of the body), Malaise (sense of discomfort), Muscle cramps, Nausea, Osteoarthritis, localized (in another area), Osteoarthritis, aggravated (made worse), Pain in lower limb (leg, hip), Paresthesia (numbness, tingling), Phlebitis (inflammation of a vein), Respiratory difficulty, Skeletal pain (bone pain), Skin irritation or pruritis (itching) and Tendonitis (irritation of tendon).

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. Have radiographic evidence within the prior 6 months, as shown in the radiology reports, of OA grade 2 or 3 in one knee using Kellgren-Lawrence Grading for OA, and verified by the enrolling physician.
a. Grade 2 defined as definite osteophytes with unimpaired joint space.
b. Grade 3 defined as definite osteophytes with moderate joint space narrowing.
2. Subjects are required to be on routine pain medication (at least 5 of the last 7 days) at screening.
3. Treatment knee criteria:
a. WOMAC Pain subscale score of 4-8 points on a NRS 3.1 Index (where 0= no pain and 10= worst pain) for the average of the five pain questions with routine medication for at least 5 of the last 7 days.
b. An increase of 1 point at baseline (after 4 days washout) for Subjects on pain medication at

screening (WOMAC Pain subscale score of 5-9 after washout).
4. Non-treatment knee average WOMAC Pain subscale score <=3 points at baseline.
5. Symptoms in the treatment knee for at least 12 months.
6. Fully ambulatory Subject (ability to perform a 15 meters walk test).
7. Male and female Subjects 40 through 85 years of age.
8. Willing to use only acetaminophen (paracetamol) (up to 3 grams/day) for pain relief during the duration of the study.
9. Written consent to participate in the clinical study following Subject*s review of the COR1.1 Study Subject Information and Consent Form.
10. Able to understand the requirements of the study and willing to comply with all treatment and study evaluations for the duration of the trial.
11. If female, must use a medically acceptable form of contraception for at least 1 month prior to Screening and continue use for the duration of the study . Otherwise, females must be surgically sterile, or postmenopausal (as documented in medical history) for at least 1 year.
12. Have completed the pain and OA medication washout period.
13. Willing to abstain from any pain medications for 24 hours prior to all study visits.

Exclusion criteria

1. Non-treatment knee joint pain >3 points average WOMAC Pain subscale scores.
2. Any Subject with an increase in WOMAC A pain subscale score of <1point after 4 day wash-out period.
3. Secondary OA (acute knee injury, rheumatoid arthritis, history of joint infection, chondrocalcinosis, osteonecrosis, chronic fibromyalgia) or other chronic autoimmune disease.
4. Generalized symptomatic OA in 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 x-rays. Upper extremity OA is NOT excluded.
5. Significant valgus/varus deformities, ligamentous laxity, or meniscal instability as assessed by the Investigator.
6. Active infection in either knee joint or adjacent tissues or positive synovial fluid culture of any joint.
7. Any contraindications for IA injection or aspiration.
8. Knee surgery or trauma within 3 months prior to enrollment or planned joint surgery for the period of study duration.
9. IA steroid injection in the knee and/or use of systemic (oral) corticosteroids within 3 months prior to enrollment. Inhaled steroids are NOT excluded.
10. IA hyaluronan injection in the treatment knee within 6 months prior to enrollment.
11. BMI >40.
12. Known hypersensitivity/allergic/anaphylactic reactions to local anesthetics.
13. Known sensitivity to corticosteroids, or hyaluronan-based products.
14. Arthroscopy of either knee or in any other joint within 3 months prior to enrollment.
15. Uncontrolled diabetes, uncontrolled hypertension or active infection end-state hepatic or renal disease; or Subjects on immunosuppressive therapy.
16. Current use of IA injections.

17. Current use of any systemic steroid therapies (oral, IV or IM), inhaled steroids are permitted.
18. Initiated a physical therapy or exercise regime within 3 months prior to enrollment.
19. Use of braces within 3 months prior to enrollment or planned use of braces for the period of study duration.
20. Clinically significant conditions that would interfere with accuracy of study evaluations including but not limited to:
a. Fibromyalgia
b. Chronic Fatigue Syndrome
c. Gout
d. Malignant neoplastic disease
e. IA tumor
f. Peripheral neuropathy
g. Vascular insufficiency
h. Hemiparesis
i. Baker's cyst
20. History, diagnosis, signs or symptoms of any clinically significant psychiatric disorder, including but not limited to:
a. Bipolar disorders
b. Psychotic disorders
c. Depression with hospital admission within last 5 years
d. Suicide attempt within last 5 years
e. Active alcohol/drug abuse within last 2 years
f. Any other factors that the investigator feels would interfere with study evaluations and study participation
21. Subjects on anti-depressive medications for significant depression or anxiety.
22. Participation in another clinical trial and/or treatment received with any investigational agent within 30 days before enrollment.
23. Active asthma that may require periodic treatment with systemic steroid during the study period.
24. Ongoing litigation for workers compensation for musculoskeletal injuries or disorders.
25. Planned/anticipated surgery of the treatment knee during the study period.
26. Female Subjects who are pregnant and/or nursing or planning a pregnancy during the course of the trial.

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):	01-10-2013
Enrollment:	210
Type:	Anticipated

Medical products/devices used

Generic name:	Intra- Articular injection of Hydros / Hydros TA Joint Therapy
Registration:	No

Ethics review

Approved WMO Date:	22-10-2013
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	25-04-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	07-10-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen

	(Wijchen)
Approved WMO Date:	21-11-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	15-02-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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
Other	Het NCT nummer is aangevraagd en zal worden aangeleverd zodra beschikbaar
CCMO	NL45893.072.13