The Orthokin trial, a prospective double blind placebo controlled randomized trial to investigate the effectiveness of autologous Interleukin-1 receptor antagonist in the treatment of osteoarthritis (OA).

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22051

Source
NTR

Brief title
N/A

Health condition

OA of the knee.

Sponsors and support

Primary sponsor: Dr. D.B.F. Saris
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Source(s) of monetary or material Support: SOMAS

Intervention

Outcome measures

Primary outcome

Questionnaires.

Secondary outcome

X-rays.

Study description

Background summary

Osteoarthritis (OA) is a slowly progressive degenerative disease, which can induce pain and functional impairment and is therefore disabling. Eventually, the disease can progress to such a state that total joint replacement or arthrodesis is the only effective treatment option.

Over the past 1-2 decades many studies have shown that inflammatory cytokines play an important role in the development and progression of OA. Interleukin-1beta (IL-1□) has often been suggested to play a key role in this process. Orthokin® is an autologous treatment containing high amounts of Interleukin-1 receptor antagonist (IL-1ra) that is induced by stimulation of the patients own blood by “surface treated” glass particles. IL-1ra is a natural inhibitor of IL-1□ as it binds to the IL-1 receptor, thereby preventing the binding of IL-1□ and inhibiting the acitvation of the receptor.

This double blind prospective placebo-controlled randomized trial will investigate the effectiveness of Orthokin□ (an autologous Interleukin-1 receptor antagonist) in the treatment of symptoms and the prevention of progression of OA.

150 patients with knee osteoarthritis (grade 1-3) will be enrolled in this study and will be randomized for treatment either with Orthokin or with a placebo (physiological saline). The randomization will be stratified to gender and to age (below 45 years old, between 45 and 65 and over 65 years old). The treatment for the patients in both groups will be identical to ensure that both the patient and the treating surgeon are blinded for the treatment the patient received. The treatment comprises a venapunction to obtain 50 milliliters of blood using the Orthokin® syringe containing the “surface treated” glass particles. This blood send to the Orthogen laboratory where it is prepared for intra-articular injection. The patients will receive 6 intra-articular injections over a period of 4 weeks, either with Orthokin® or with a placebo. Before administration of the treatment, the synovial fluid present in the treated joints will be collected to prevent dilution of the drug and for measurement of the concentrations of various inflammatory cytokines by multiplex ELISA (Biorad®). Before and 3, 6, 9 and 12 months after the initiation of the treatment, the patients will be asked to fill out a questionnaire (containing a VAS for pain, the Knee injury and Osteoarthritis Outcome Scale (KOOS) and the 100-point knee society clinical rating scale) to evaluate the effectiveness of the treatment. At these time-points the patients will also be asked to return to the outpatient clinic for objective evaluation of the effectiveness of the treatment by their treating surgeon. 12 months after initiation of the treatment is the primary endpoint of this study as the effectiveness of the treatment with respect to the symptomatology of OA will than be evaluated.

As OA is a slowly progressive disease, the patients will be asked to return to the outpatient clinic five years after initiation of the treatment, to evaluate whether a real long-term protective effect by this treatment can be observed. During this visit a physical exam and X-rays (as previously described) will be done to assess the disease progression objectively. Three independent investigators, who are blinded to the treatment, will evaluate all X-rays (Baseline, 1 year follow-up and 5 year follow-up X-rays) according to the Kellgren and Lawrence radiological assessment scale for osteoarthritis. Patients who received surgery over the last five years in the affected joint will be excluded from analysis. If this surgery was related to OA, the treatment will be considered a treatment failure and will be assigned to Kellgren and Lawrence grade IV. Usage of NSAID’s, oral corticosteroids and intra-articular injections with corticosteroids and hyaluronic acid will be taken into account and will be sub-classified on analysis.

Study objective

1. Orthokin relieves symptoms of pain and dysfunction of OA as determined by the outcome of designated subjective scoring systems;

2. Orthokin reduces inflammatory markers in synovial fluid;

3. Orthokin inhibits long-term radiological progression of OA development.

Study design

N/A

Intervention

Inclusion interview, X-rays of the knee and filling out questionnaires.

Vena punction.

Six intra-articular injections of the afflicted
knee with Orthokin or placebo.

Every 3 months visiting treating physician with questionnaires. At 12 months again radiographs.

Contacts

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Eligibility criteria

Inclusion criteria

1. Typical symptoms for osteoarthritis as judged by the physician;

2. Previous treatment more than 6 months ago;

3. Patient signed informed consent;

4. Patient > 18 years old;

5. Minimal 40 mm VAS pain;

6. Maximal 60 points Knee Society Rating Scale;

7. Maximal 60 points KOOS index.

Exclusion criteria

1. Participation in concurrent trials;

2. Participation in previous trials within 3 months;

3. Patient know with HIV, Hepatitis, CMV and Syphilis infections;

4. Alcohol and drug abuse;

5. Poor general health condition as judged by the treating physician;

6. Received hyaluronic acid and/or corticosteroid intra-articular injections into the afflicted knee within the last 6 months of baseline;

7. Intake of specific drugs, such as chondroitin sulfate, diacerein, n-glucosamine, piacledine, capsain within 2 weeks of the baseline visit;

8. Any concomitant painful or disabling disease of the spine, the hips or lower limbs that would interfere with evaluation of the afflicted knee;

9. Ipsilateral coxarhrosis and hip prothesis loosening;

10. Any clinically significant or symptomatic vascular or neurological disorder of the lower extremities;

11. All crystalline, inflammatory and infectious arthropathies;

12. Current diagnosis of osteomyelitis.

OA grade IV;

13. Known immunodeficiency;

14. Corticosteroid usage;

15. Anti-coagulant usage and coagulopathy;

16. Morbid obesity.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2004
Enrollment:	182
Type:	Actual

Ethics review

Positive opinion

Date:	12-09-2005
Application type:	First submission

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
NTR-new	NL166
NTR-old	NTR202
Other	: N/A
ISRCTN	ISRCTN44912979

Study results

Summary results
N/A