Placebo controlled trial to evaluate the effect on pain and function of six months treatment doxycycline in established knee osteoarthritis with an open extension up to two years

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To asses the short and long term effect on pain and function and the safety of doxycycline in patients with mild to severe pain due to established knee OA.

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

Summary

ID

NL-OMON31361

Source
ToetsingOnline

Brief title
Symptomatic treatment with doxycycline in established knee osteoarthritis

Condition

- Joint disorders

Synonym
OA, osteoarthritis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: reumafonds;eigen RDE afdeling

Intervention

Keyword: controlled trial, doxycycline, knee osteoarthritis, tetracyclin

Outcome measures

Primary outcome

Percentage of the patients achieving clinical response on pain and function, as defined by the OMERACT-OARSI set of responder criteria compared to placebo at week 24

Secondary outcome

Percentage of the patients achieving clinical response on pain and function, as defined by the OMERACT-OARSI knee OA response criteria at week 96.

Mean KOOS pain sumscores question 5 to 9, function sumscore question 1 to 17 and VAS patient Global Assessment compared between baseline, week 24 and week 96.

Safety (adverse events graded according to the CTC criteria)

The rate of JSN in the medial knee compartment at week 96 as assessed by the Lequesne scoring method (21)

Study description

Background summary

Knee osteoarthritis (Knee OA) is a prevalent chronic disease characterized by cartilage failure resulting in pain, stiffness and function loss.
Symptomatic treatments for knee OA include medical treatment with analgesics (acetaminophen) and NSAIDs, paramedical treatment including occupational and physical therapy, weight reduction, and eventually joint replacement. Although NSAIDs have been extensively studied and used for OA, there are some important drawbacks to consider like inefficacy and gastrointestinal and cardiovascular safety issues and possibly increased progression of knee OA. Therefore the search for a DMAOD with both symptomatic and structural effects has been intensified in recent years.
Doxycycline is a tetracycline class antibiotic agent. Besides being an antimicrobacterial agent, it is a metalloproteinase inhibitor and inhibits the collagenase that splices collagen type IX that is present in articular cartilage. Doxycycline has been studied in human OA in one clinical trial by Brandt et al. Although effect on structural change has been shown for doxycycline, whether it also modifies symptoms for osteoarthritis has not been established yet. Side effects were mild and drop-out due to side effects was rare (<5%).
A possible beneficial effect of doxycycline on pain and function in knee OA would allow this drug to be introduced in the non-invasive treatment of knee OA for both symptomatic and structural benefit. Because doxycycline is not associated with the important adverse effects of NSAIDs like gastrointestinal and cardiovascular morbidity and mortality this could be of high clinical relevance. In addition, doxycycline can be expected to have a beneficial effect on cartilage compared to the possible deleterious effect of NSAIDs on cartilage.

Study objective

To asses the short and long term effect on pain and function and the safety of doxycycline in patients with mild to severe pain due to established knee OA.

Study design

Randomized, double blind placebo controlled trial (24 weeks) with open extension (96 weeks).

Intervention

Doxycycline monohydrate 2dd100mg or Placebo for 24 weeks, thereafter open label

doxycycline monohydrate 2dd100mg

Study burden and risks

The experienced burden for patients included in this study is low. The intervention has been shown to be safe and has excellent tolerability. Patients will be taking two pills daily, and will be expected to visit the hospital every three months in the placebo phase and every six months in the open extension phase (with telephonic consultation in between). The outcome measures are widely accepted and short questionnaires, routine safety blood tests and standard x-rays at three time points.
Possible benifits include symptomatical relief by doxycyclin and delayed progression of asteoarthritis.

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

· Knee OA (index knee) according to the 1986 proposed ACR classification tree using clinical and radiological criteria: knee pain (VAS > 40mm during > 50% of last month), the presence of osteophytes and one of the following: age >50, crepitus, or morning stiffness < 30 minutes.
· Kellgren Lawrence score II or III
· Criteria for mild to severe pain (KOOS pain sumscore question 5 to 9 > 100 in the index knee) must be fulfilled
· Ability to read and communicate well in Dutch.

Exclusion criteria

· Other rheumatic diseases like rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematodes or psoriatic arthritis.
· The presence of secondary OA including OA caused by orthopaedic problems (severe malalignment, trauma), ochronosis, acromegaly, calcium pyrophosphate deposition disease (CPPD), haemochromatosis.
· Severe functional problems related to diseases other than OA (functional class ARA IV)
· Cognitive deficits affecting the scoring processes.
· Severe OA (Kellgren Lawrence score IV)
· Ipsilateral hip prosthesis in situ.
· Contraindications for doxycycline use like allergy for tetracyclines and prior adequate treatment with doxycycline (>100mg for > 6 weeks for OA).
· Planned other major interventions within 24 weeks, including lower limb surgery and intensive multidisciplinary approaches.
· Recent intra-articular hyaluronic acid or corticosteroid application (<3 months) or surgery (<1 year) in the index knee.
· Recent participation in other study (< 3 months)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2007
Enrollment:	230
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	doxycycline
Generic name:	doxycycline
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	21-08-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2007-001151-19-NL
CCMO	NL16884.091.07