A Multicenter, Randomized, Double-Blind, Placebo- and Active-Controlled Study Comparing the Safety and Analgesic Efficacy of ABT-110 to Placebo in Subjects with Pain from Osteoarthritis of the Knee

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON37475

Source
ToetsingOnline

Brief title
M12-146

Condition

- Joint disorders

Synonym
ostheoarthritis, pain

Research involving

Human

Sponsors and support

Primary sponsor: AbbVie B.V.
Source(s) of monetary or material Support: AbbVie BV

Intervention

Keyword: Anti-Nerve growth Factor, Osteoarthritis, Pain

Outcome measures

Primary outcome

Efficacy: Efficacy assessments will include the following: Subjects Assessment of Arthritis Pain Intensity by VAS (100 mm), Western Ontario and McMasters Osteoarthritis Index (WOMAC*), EuroQol-5D* (EQ-5D-5L), Work Productivity and Activity Impairment (WPAI) Questionnaire, Subject's Global Assessment of Arthritis Status, and Subject's Global Assessment of Study Drug.

Safety: Safety will be monitored throughout the study based on assessments of adverse events (AEs), physical examinations, neurological exams, vital signs, radiographic exams and laboratory values. Additionally, an Independent Data Monitoring Committee (IDMC) will monitor the safety data in an unblinded fashion, with a particular focus on AEs of special interest (AESI).

Secondary outcome

Pharmacokinetic: Serum samples for ABT-110 PK and ADA testing will be obtained during the study. Values for the pharmacokinetic parameters of ABT-110 including apparent clearance (CL/F) and apparent volume of distribution (V/F) will be estimated using population pharmacokinetic modeling procedures.

Study description

Background summary

Osteoarthritis is a syndrome of joint pain accompanied by varying degrees of functional limitation and reduced quality of life. It is the most common disease of the joints. Symptoms can vary from minimal to severe pain and stiffness but overall the disease is responsible for considerable morbidity and is noted to be difficult to treat. The guidelines for the management of knee OA advocate lifestyle changes such as weight loss and local muscle strengthening as well as analgesics on an as required basis.
However, currently available therapies have limitations, including inadequate efficacy, dose-limiting side effects, and medical conditions precluding use of therapy. Moderate to severe knee OA pain is therefore a condition for which a new, effective pharmacological intervention would be of considerable clinical value.

One of the most promising novel targets is that of nerve growth factor (NGF). ABT-110 is a humanized anti-nerve growth factor (anti-NGF) monoclonal antibody that prevents the binding of NGF to its receptors. AbbVie proposes to study ABT-110 in adults with moderate to severe pain due to moderate OA of the knee.

Study objective

The primary objective for this study is to compare the safety, tolerability and analgesic efficacy of ABT-110 administered subcutaneously (SC) once every 8 weeks (q8w) for a total of 2 doses to placebo in subjects with pain due to osteoarthritis (OA) of the knee.
A secondary objective is to explore the population pharmacokinetics of ABT-110.

Study design

This is a Phase 2, multicenter, randomized, double-blind, placebo- and active-controlled parallel-group study designed to compare the safety, tolerability and analgesic efficacy of ABT-110 administered by SC injection q8w for a total of 2 doses, to placebo in subjects with pain from OA of the knee. Naproxen 500 mg BID is included for assay sensitivity.

Intervention

At baseline, subjects are randomized to 1 of 6 arms. All subjects receive subcutaneous injections (1 ml in total) in the abdominal area on Day 1 and week 8 visit. Depending on the arm in which the subject is randomized this injection will contain 1 mg, 5 mg, 10 mg or 20 mg ABT-110 or placebo. In addition,

subjects will take naproxen or placebo capsules twice a day.

Study burden and risks

The risks associated with this study are linked together with the possible side effects of the investigational product and naproxen.
The burden of the subject will continue to work with the study procedures, visits, and venapunctions. All subjects will be closely monitored and supervised by experienced doctors and study staff for possible side effects.

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

• you are between 18 and 70 years of age, inclusive;
• Osteoarthritis in the index knee adapted from the American College of Rheumatology Clinical and Radiographic Criteria for Ostheoarthritis of the knee: History of pain in the index knee >= 6 months; AND Kellgren and Lawrence (K-L) Grade 2 or 3 only, on plain radiographs of the index knee; AND At least 1 of the following 3 criteria:* Age > 50 years; OR * Stiffness < 30 minutes upon awakening; OR * Crepitus in the index knee.
• You must meet the following pain criteria at Baseline Visit: 1. Subject*s Assessment of Arthritis Pain Intensity (VAS) of the index knee is >= 40 mm with an increase of >= 10 mm from Screening Visit,
o For subjects whose Screening VAS is >= 85 mm, a VAS of >= 85 mm must be maintained at the Baseline Visit; AND
2. Subject's Global Assessment of Arthritis Status must be Fair, Poor or Very Poor.
• you require therapeutic doses of at least 1 of the following oral analgesics for OA pain during the previous 3 months, with a stable dose for at least 4 days per week during 4 weeks prior to Screening:
* NSAIDs
* COX-2 inhibitors
* Tramadol or tapentadol
* Opioids (alone or in combination products)

Exclusion criteria

• Is scheduled for or is considering joint replacement surgery at any time during the study (including the Follow-up Period and the Post-Study Follow-up Period).
• Has had any of the following: Joint replacement/reconstruction either knee at any time; OR Any major surgery, e.g., open surgery, to the index joint within the 12 months prior to the Screening Visit; OR Arthroscopic surgery to the index joint within 3 months prior to the Screening Visit; OR Trauma to the index knee within 12 months prior to the screening visit.
• Has a history of osteonecrosis (ON) or rapidly progressive osteoarthritis (RPOA) in any joint.
• Has OA of the index knee that meets K-L classification criteria of grade 0, 1 or 4. Subject has OA of the contralateral knee that meets the K-L classification of grade 4.
• Has radiographic evidence (K-L grade >= 2 based on central radiologist interpretation of screening radiographs) of OA of the hip or shoulder joints.
• Prior to the Screening Visit, has received: Oral corticosteroid therapy for a duration of > 2 weeks continuously or a total exposure of > 2 weeks (e.g. > 1 week of treatment on 2 or more separate occasions) within the previous 2 years; OR Intramuscular, intravenous or epidural corticosteroid therapy within the previous year; OR intra-articular injection of corticosteroids within the previous year; OR intra-articular injection of Synvisc (hyaluronic acid) in the index knee within the previous year.
• Has a history of clinically significant sensitivity or allergy to:
paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs); and/or has a history of injection site reaction or formation of anti-drug antibodies to a biologic compound.
• Has a diagnosis of any of the following painful syndromes/conditions:
- Inflammatory arthritides, such as rheumatoid arthritis (including juvenile rheumatoid arthritis), seronegative spondyloarthropathy or pseudogout;

- History of infectious arthritis involving the index joint;
- Clinically active gout within 3 months prior to the Screening Visit;
- Paget's disease;
- Fibromyalgia;
- Neuropathic pain; or
- Any other chronic painful syndrome(s)/condition(s) that could interfere with the assessment of pain in the index joint.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	ABT-110
Generic name:	ABT-110
Product type:	Medicine
Brand name:	Naprosyn
Generic name:	Naproxen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-10-2011
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	02-07-2012
Application type:	First submission
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	05-07-2012
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	16-08-2012
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	22-10-2012
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)
Approved WMO Date:	04-12-2012
Application type:	Amendment
Review commission:	METC Slotervaartziekenhuis en Reade (Amsterdam)

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	EUCTR2011-002144-27-NL
CCMO	NL38298.048.11