A Phase 2a, multicenter, randomized, double-blind, placebo-controlled study to compare the safety and efficacy of ABT-981 to placebo in subjects with erosive hand osteoarthritis

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

Summary

ID

NL-OMON42110

Source
ToetsingOnline

Brief title
M14-171

Condition

- Joint disorders

Synonym
ostheoarthritis, pain

Research involving
Human

Sponsors and support

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

Intervention

Keyword: and IL-1&beta, Erosive hand osteoarthritis, IL-1&alfa, inhibitor, Pain

Outcome measures

Primary outcome

The primary efficacy measurement will be the change of pain from Baseline to 16

weeks as assessed by the AUSCAN NR3.1 pain subdomain score.

Secondary outcome

* Change of total AUSCAN score and individual subdomain (pain, physical

function and stiffness) scores from Baseline using the AUSCAN NR3.1.

* Change of subject index hand resting pain from Baseline using NRS-11 score.

* Change of patient global assessment of arthritis from Baseline using NRS-11

score.

Study description

Background summary

Osteoarthritis (OA) is a joint disorder that involves degeneration of articular cartilage, inflammation of the entire joint as manifested by synovitis, and changes in the subchondral bone. OA is the most common form of arthritis and the number one cause of workforce disability.
The importance of inflammatory elements in OA is increasingly recognized; the role of cytokines and chemokines as the "inflammatory"
mediators that cause inflamed synovial tissue and cartilage in OA have been extensively studied.

Among these inflammatory mediators, Interleukin-1 (IL-1) is identified as the key factor in cartilage and synovium tissue signaling pathways. IL-1 has long

been known as the most potent catabolic cytokine and is thought to play a major role in the development and progression of OA both in terms of disease (structural progression) and symptoms (pain and functional deterioration).

IL-1α and IL-1β are 2 structurally distinct cytokines that bind to the IL-1 receptor complex. Both induce structural changes, such as cartilage degradation, bone sclerosis and synovial proliferation, by inducing proteases and proinflammatory cytokines in joints and have also been shown to play a role in OA pain.
ABT-981 is a novel biologic drug candidate targeting IL-1α and IL-1β.

Study objective

Primary
The primary objective is to evaluate the effect of ABT-981 on pain using the Australian/Canadian Osteoarthritis Hand Index (AUSCAN NR3.1) pain subdomain score, in subjects with erosive hand OA at Week 16.

Secundary
* Evaluate the safety and tolerability of ABT-981 in subjects with erosive hand OA throughout the study.
* Evaluate the effect of ABT-981 on AUSCAN NR3.1 total and individual subdomain (pain, physical function and stiffness) scores of erosive hand OA throughout the study.
* Evaluate the effect of ABT-981 on Subject Assessment of Hand Pain Intensity via an 11-point Numeric Rating Scale (NRS-11) throughout the study.
* Evaluate the effect of ABT-981 on Patient Global Assessment (PGA) of Hand Osteoarthritis Status using a NRS-11 throughout the study.
* Evaluate the PK and ADA levels of ABT-981.

Study design

This is a Phase 2a, multicenter, randomized, double-blind, placebo-controlled, parallel group study designed to evaluate the safety, tolerability, efficacy, PK and pharmacodynamics (PD) of ABT-981 compared to placebo in subjects with erosive hand OA.

Approximately 120 subjects meeting the selection criteria will be randomized into the study at approximately 45 sites.

The duration of the study and subject participation will be approximately 32 weeks. The study consists of 2 periods: 1) a Screening and Washout Period for approximately 45 days prior to first dose; 2) a 26-Week Study Period.

Intervention

Approximately 120 patients meeting all of the inclusion criteria and none of the exclusion criteria during Screening (within 45 days prior to the first dose of study drug) will be enrolled. Patients taking analgesics must complete a Washout Period and discontinue all analgesic medications for at least 5 half-lives of the longest acting analgesic used, or 48 hours, whichever is longer, prior to the first dose of study drug. Upon completion of the wash-out period, the baseline MRI should be performed 7 - 17 days prior to Day 1. During the Washout Period through Week 26 it is permitted to take acetaminophen as rescue mediation, but not within 48 hours prior to MRIs and visits with questionnaires.

Patients will be randomized to one of the two treatment groups to receive either placebo or 200 mg ABT-981 every other week for 26 weeks (treatment period).
Patients will undergo 2 X-rays and 2 MRIs during the study.

Study burden and risks

The risks associated with this study are linked together with the possible side effects of the investigational product. 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

1. Male or female between the ages of 35 to 80 years (inclusive) at the time of signing the informed consent.
2. Subject must fulfill 1990 American College of Rheumatology (ACR) hand OA criteria, defined as
hand pain, aching, or stiffness and three or four of the following features:
* hard tissue enlargement of two or more of the following 10 selected joints: the second and third distal interphalangeal (DIP) joint of both hands, the second and third proximal interphalangeal (PIP) joints of both hands, the first carpometacarpal (CMC) joints of both hands,
* hard tissue enlargement of two or more DIP joints,
* fewer than three swollen metacarpophalangeal (MCP) joints, and
* deformity of at least one of the 10 selected joints.
3. Subject must have radiographic evidence of erosive hand OA with evidence of an "E" (erosive) or "E/R" (erosive with remodeling) joint as defined by Verbruggen and colleagues in at least one of the hand interphalangeal joints based on hand x-rays obtained during the Screening Period or within 3 months of the Screening Visit (a qualified central reader will perform the eligibility reading
according to a pre-defined criterion).
4. Subject has one or more clinical signs and symptoms of active inflammation in at least three hand joints, with active inflammation defined as localized tenderness and/or soft tissue swelling at Screening and Day 1 Visit.
5. Subject Assessment of Hand Pain Intensity in at least one hand is >= 6 (11-point Numeric Rating
Scale [NRS-11]) at Screening and Day 1 Visit.
6. Patient Global Assessment of Arthritis Status is >= 6 (NRS-11) at Screening and Day 1 Visit.

Exclusion criteria

1. Previous exposure to any anti-IL-1 treatment including (and not limited to) anakinra, canakinumab and rilonacept OR one or more of the following:

* Oral, intramuscular (IM), intravenous (IV), epidural or intra-articular corticosteroids within 1 month prior to Screening,
* Intra-articular hyaluronic acid injection into hand joint(s) within 6 months prior to Screening,
* Any investigational drug product of chemical or biologic nature within 1 month or 5 half-lives
of the drug (whichever is longer) prior to the first dose of study drug,
Any immunosuppressive biologic therapy including (and not limited to), etanercept, adalimumab, infliximab, golimumab, certolizumab, abatacept, tocilizumab, natalizumab, efalizumab, ustekinumab, belimumab or rituximab within 1 month or 5 half-lives (whichever is
longer) prior to the first dose of study drug,
* Current use of immunosuppressive oral medications including (and not limited to) Tofacitinib,
hydroxychloroquine, azathioprine, methotrexate, leflunomide, mycophenolate, sulfasalazine, gold, cyclophosphamide, penicillamine and/or tacrolimus, or tetracycline based agents within 3 months or 5 half-lives (whichever is longer) prior to the first dose of study drug,
* Colchicine within 1 month prior to the first dose of study drug,
* Vaccination with a live viral agent (including live attenuated influenza vaccine via nasal spray)
<= 30 day prior to Screening Visit through 10 weeks (5 × the half-life of ABT-981) after the last
dose of study drug.
2. Absolute neutrophil count (ANC) < 2,000/mm3 at Screening.
3. Diagnosis of one or more of the following:
* Fibromyalgia,
* Inflammatory arthritis such as rheumatoid arthritis, peripheral seronegative spondyloarthropathy,
* Psoriatic arthritis, evidence of psoriasis,
* Microcrystalline (including gout and pseudo gout) arthritis affecting the hands,
* Any OA of the hands due to an infectious origin or acute traumatic episode,
* Secondary OA due to (but not limited to) hemochromatosis, alkaptonuria, Wilson's disease, acromegaly and/or hyperparathyroidism,
* OA linked to cartilage and bone dysplasia,
* Other chronic painful syndromes that could interfere with assessment of pain at the hand(s).
4. Any uncontrolled medical illness or an unstable treatment or therapy.
5. Clinically significant cardiac disease (including MI, coronary stenting or CVA) within last 12 months of Study Day 1 or clinically significant findings at Screening ECG including QT interval corrected for heart rate by Fridericia's formula (QTcF) > 470 msec in females or > 450 msec in males or PR interval > 220 msec.
6. Evidence of dysplasia or history of malignancy (including lymphoma and leukemia) within the past
5 years other than a successfully treated non-metastatic cutaneous squamous cell or basal cell
carcinoma or localized carcinoma in situ of the cervix.
7. History of persistent chronic or active infection(s) requiring hospitalization or treatment with

antimicrobials/antibiotics (intravenous, oral, or injection) within 1 month prior to the first dose of
study drug.
8. Any reason that prohibits a subject to undergo an MRI (e.g., pacemaker, certain types of metal
implants, etc.). The number of subjects not undergoing an MRI will be limited to 10 per arm

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:	Recruitment stopped
Start date (anticipated):	10-09-2015
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ABT-981
Generic name:	ABT-981
Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo

Ethics review

Approved WMO Date:	05-02-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-05-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-09-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	17-09-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2014-001096-31-NL
CCMO	NL51904.058.15