A PHASE I/II, MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY, WITH A SINGLE ASCENDING DOSE PART FOLLOWED BY A MULTIPLE ASCENDING DOSE PART, EVALUATING THE SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS AND EFFICACY OF INTRAVENOUS ALX-0061 IN PATIENTS WITH RHEUMATOID ARTHRITIS

Published: 22-12-2010
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Primary:to investigate the safety and tolerability of single and multiple doses of the study drug given by intravenous injection/infusion to patients with RAto determine the maximum tolerated dose and/or biologically effective dose of the study...

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

Summary

ID

NL-OMON36644

Source
ToetsingOnline

Brief title
ALX-0061 phase I/II, SAD and MAD study in RA patients

Condition

- Autoimmune disorders
- Joint disorders

Synonym
chronic joint inflammation, Rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Ablynx
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ALX-0061, rheumatoid arthritis

Outcome measures

Primary outcome

Pharmacodynamics

Pharmakinetics

Efficacy

Safety parameters

Secondary outcome

NA

Study description

Background summary

The study medication to be given is a new, investigational compound that may eventually be used for the treatment of rheumatoid arthritis. Rheumatoid arthritis is a long-term inflammatory disease affecting the whole body but principally attacks the joints producing an inflammatory reaction that often

progresses to destruction of the joints. Although the cause of rheumatoid arthritis is unknown, autoimmunity (where the body defense system does not respond in the correct way) plays a key role in production of symptoms and progression of the disease. In patients with rheumatoid arthritis high concentrations of IL-6, an inflammatory marker, are found. The investigational drug is a therapeutic antibody for the treatment of rheumatoid arthritis by means of inhibition of the receptor for IL-6.

Study objective

Primary:
to investigate the safety and tolerability of single and multiple doses of the study drug given by intravenous injection/infusion to patients with RA
to determine the maximum tolerated dose and/or biologically effective dose of the study drug

Secondary:
to determine the efficacy of multiple dosing with the study drug in patients with RA
to investigate the pharmacokinetics of the study drug after single and multiple dosing in patients with RA
to investigate the pharmacodynamics of the study drug after single and multiple dosing in patients with RA
to investigate the immunogenicity of the study drug after single and multiple dosing in patients with RA

Study design

Design:
a multi-center, randomized, double-blind, placebo controlled, dose-escalation, phase I/II study in patients with RA, consisting of a SAD part and a MAD part. The SAD part will consist of 1 group (Group 1) of 4 (2+2) patients and up to 4 groups (Groups 2-5) of 8 (6+2) patients each. In each group, as of the second group, 6 patients will receive a single intravenous (iv) dose of the study drug and 2 patients will receive a single iv dose of placebo.

Procedures and assessments
clinical laboratory, vital signs (including oral body temperature), physical examination, body weight, abdominal ultrasound, ACR classification of functional capacity and DAS 28, 12-lead ECG, pregnancy test (females only); at eligibility screening: medical history, body height, chest X-ray, Quantiferon test for active tubercolosis, blood sampling for PD biomarkers, blood sampling for immunogenicity assessment, , alcohol and drug screen, HBsAg, anti HCV, anti-HIV 1/2; alcohol and drug screen, pregnancy test (females only), immunogenicity assessment, ACR classification of functional capacity and ACR assessment of criteria for ACR response, DAS28 score, disease activity VAS and

HAQ to be repeated upon admission

Observation period
one period in clinic from Day -1 up to 48 h or 72 h (based on the judgement of the Investigator) after drug administration on Day 1 and ambulatory visits on Days 4, 5, 8, 15, 29, 36, 57 and follow-up

Blood sampling
for pharmacokinetics of ALX-0061 in plasma: pre-dose and at end of injection/infusion and 8 h post-dose and once on Days 2, 3, 4, 5, 8, 15, 29, 36, 57 and once at follow-up
for pharmacodynamic parameters (CRP, ESR and fibrinogen, IL-6, sIL-6R, TNF-*, IL-1* and IFN-*: pre-dose and 8 h post-dose and once on Days 2, 3, 4, 8, 15, 29, 36, 57 and once at follow-up
for immunogenicity: pre-dose and once on Days 8, 15, 29 and 57 and once at follow-up

Efficacy assessments
ACR reponse, DAS 28 score, EULAR response, disease activity VAS and HQ: once on Day 57

Safety assessments
Adverse events: throughout the study; vital signs pre-dose and 1, 2, 4 and 8 h post-dose and once on Days 3, 4, 8, 15, 29, 36 and 57; 12-lead ECG: pre-dose and 2 and 8 h post-dose and once on Days 8, 15, 29, 36 and 57; clinical laboratory: pre-dose and once on Days 8, 15, 29, 36 and 57

Bioanalysis
analysis of serum ALX-0061 samples using a validated method by Sponsor
analysis of serum anti-ALX-0061 antibodies samples using a validated method by Sponsor
analysis of CRP, ESR and fibrinogen using a clinical chemistry method by PRA
analysis of serum SAA samples using a validated method by PRA
analysis of serum IL-6 samples using a validated method by PRA
analysis of serum TNF-*, IL-1* and IFN-* samples using validate methods by PRA

Intervention

Active substance: ALX-0061
Activity: anti-interleukin-6 receptor (IL-6R) nanobody inhibitor
Indication: rheumatoid arthritis
Dosage form: solution for injection/infusion

Study burden and risks

Procedures: pain, light bleeding, haematoma, possibly an infection.

Contacts

Public
Ablynx

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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. Gender: male and female
2. Age: 18-80 years, inclusive
3. Body mass index (BMI): <35.0 kg/m2
4. Diagnosed with RA according to the 2010 European League Against Rheumatism (EULAR)/ American College of Rheumatology (ACR) criteria for at least 6 months prior to randomization
5. Inadequate response or intolerance to disease modifying antirheumatic drugs (DMARDs) (including methotrexate [MTX]). Treatment with MTX for at least 12 weeks prior to screening, with at least 4 weeks before screening at a stable dose, that will remain stable throughout the study period
6. DAS28 ><= 2.4

Exclusion criteria

1. A documented history of an autoimmune disease other than RA (other than secondary Sjögren*s syndrome)
2. Functional class IV by ACR classification
3. Any new/additional biologic DMARD therapy, cytotoxic drugs and immunosuppressants within four weeks prior to screening, and between screening and Day 1 with the exception of ALX-0061
4. Suspicion of active tuberculosis verified by quantiferon test and abnormal chest X-ray
5. Female patients who are pregnant during the study, or are breastfeeding
6. History of anaphylactic reactions to protein therapeutics
7. Participation in an investigational drug study within 60 days prior to drug administration except for the patients who participated in the SAD part of this study and who are eligible to participate in the MAD part
8. Donation of more than 300 mL of blood within 60 days prior to drug administration
9. Malignancy, or prior malignancy, with a disease free interval of <5 years after diagnosis and intervention except curative treatment for non-melanoma skin cancer or resected carcinoma in situ
10. Any current or recent (within 4 weeks prior to first dose) signs or symptoms of infection that requires parenteral antibiotic administration, any known active viral infection (hepatitis B virus [HBV], hepatitis C virus [HCV], human immunodeficiency virus [HIV]) that would impair the participation in the study
11. Major surgery (including joint surgery) within 8 weeks prior to screening and hospitalization for a clinically relevant event within the 4 weeks prior to screening
12. Any other disease, metabolic dysfunction, physical examination finding, or clinically significant laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or renders the patient at high risk for treatment complications
13. Administration of a live, attenuated vaccine within 1 month before dosing with ALX-0061, or anticipation that such a live attenuated vaccine will be required during the study or within 60 days after the last dose

Study design

Design

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:	10
Type:	Actual

Ethics review

Approved WMO Date:	22-12-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2010-022865-81-NL
CCMO	NL34944.056.10