Phase I, single-centre, randomised, placebo-controlled, double-blinded study, with single ascending dose and multiple dose at maximum tolerated dose, evaluating the safety, tolerability and pharmacokinetics of ALX-0171, administered by pulmonary inhalation, in healthy male volunteers

Published: 27-10-2011
Last updated: 30-04-2024

- to determine the safety and tolerability of escalating single doses and multiple doses of ALX-0171- to evaluate the dose-limiting toxicity (DLT) level of ALX-0171 and determine the maximum tolerated dose (MTD)- to evaluate the PK of escalating...

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

Summary

ID

NL-OMON37342

Source
ToetsingOnline

Brief title
ALX-0171 Phase I study in healthy male volunteers

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
respiratory syncytial virus infection, virus that infect the airways

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ALX-0171, Respiratory syncytial virus infection

Outcome measures

Primary outcome

Pharmacokinetics: plasma ALX-0171 concentrations, pharmacokinetic parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination, pulmonary function

Secondary outcome

n/a

Study description

Background summary

The purpose of the study is to investigate how safe the compound is and how well the compound is tolerated when administrated by pulmonary inhalation. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body (this is called pharmacokinetics). Furthermore, the study will investigate if an immune response will occur in the body.

This study is not intended to improve your health, but is necessary for the further development of the new compound.

Study objective

- to determine the safety and tolerability of escalating single doses and multiple doses of ALX-0171
- to evaluate the dose-limiting toxicity (DLT) level of ALX-0171 and determine the maximum tolerated dose (MTD)
- to evaluate the PK of escalating single doses and multiple doses of ALX-0171
- to evaluate the effect of ALX-0171 on exploratory (safety-related) biomarkers
- to assess the systemic and local immunogenicity of ALX-0171

Study design

DESIGN:
A single-centre, randomised, placebo-controlled, double-blinded study, with single ascending dose (SAD) and multiple dose (MD) at MTD administered by pulmonary inhalation in healthy male subjects

In the first SAD cohort two subjects (one active and one placebo) will be dosed minimum 24 hours prior to the remaining two subjects (one active and one placebo), all remaining cohorts are randomised in a 3:1 ratio

Study drug escalation will be done as follows:
single doses of ALX-0171 or placebo will be escalated until a study drug related dose limiting toxicity occurs (CTCAE grade 3 or more, excluding hypersensitivity reactions) and/or until the CMD of 3 mg/kg is reached.

In case that CTCAE grade 2 treatment emerging toxicity is seen in *2/4 or *3/8 subjects or 1 or 2 DLT an additional 4 subjects (3 active and 1 placebo) will be recruited. In case a DLT is observed in * 3 Subjects, the MTD is defined as the dose level below the dose at which of subjects have experienced a DLT.

In the MD part sixteen subjects are dosed in a 3:1 ratio and dosed twice daily for five Days

SAD
PROCEDURES AND ASSESSEMENTS:
Screening and follow-up: clinical laboratory, physical examination (lung auscultation included), lung function tests (spirometry, DLCO), exploratory biomarkers: exhaled NO, 12-lead ECG, vital signs

at eligibility screening: medical history, Chest (thorax) X-ray, bronchial (methacholine) challenge test, body weight and height, drug and alcohol screen, HBsAg, anti HCV, anti-HIV 1/2, SAD 5 and 6 only: sputum induction

to be repeated upon submission: clinical laboratory, physical examination (lung auscultation included), exhaled NO, alcohol breath test

at follow up only: immunogenicity, alcohol breathe test

at second follow up (SAD 5 and 6 only): sputum induction

Observation period: one period in clinic from -17 h up to 72 h after drug administration on Day 1 followed by ambulatory visits on Days 5, 6 and 14 ± 1

Blood sampling: for pharmacokinetics of ALX-0171: pre-dose and 0.5, 1, 3, 6, 10, 12, 24, 30, 36, 48, 60, 72, 96 and 120 h post dose
for immunogenicity: pre-dose and Day 14 ± 1 post dose

Spirometry : pre-dose and 0.25, 0.5, 1, 2, 6, 10, 12, 24, 36, 48, 60 and 72 h post dose

DLCO: 10, 24, 48 and 72 h post dose

Exhaled NO: 24, 48, 72, 96 and 120 h post dose

Alcohol breath test: 96 and 120 h post dose

Safety assessments:
adverse events: throughout the study;
physical examination: 72 h post dose;
lung auscultation: pre-dose and 0.25 and 1h post dose;
vital signs: pre-dose and 0.5, 1, 12, 24, 48 and 72 h post dose;
12-lead ECG: pre-dose and 0.5, 6, 10, 12, 24, 48 and 72 h post dose;
clinical chemistry: 24 and 72 h post dose;
limited safety lab: 12 h post dose;
exploratory safety lab: pre-dose and 12, 24, 48 and 72 h post dose

MD
PROCEDURES AND ASSESSEMENTS:
Screening and follow-up: clinical laboratory, physical examination (lung auscultation included), lung function tests (spirometry, DLCO), exploratory biomarkers: exhaled NO, 12-lead ECG, vital signs

at eligibility screening: medical history, Chest (thorax) X-ray, bronchial (metacholine) challenge test, body weight and height, drug and alcohol screen, HBsAg, anti HCV, anti-HIV 1/2, sputum induction

to be repeated upon submission: clinical laboratory, physical examination (lung auscultation included), exhaled NO, alcohol breath test

at follow up only: immunogenicity, alcohol breathe test

at second follow up: sputum induction

Observation period: one period in clinic from -17 h up to 72 h after first drug administration on Day 5 followed by ambulatory visits on Days 9, 10 and 12 ± 1

Blood sampling: for pharmacokinetics of ALX-0171: pre morning dose and 0.5, 3, 6, 10, 12 (= pre second dose) and 4 h post second dose on Day 1 and pre morning dose on Days 2-4 and pre morning dose on Day 5 and 1, 3, 6, 10, 12, 16 and 24 h (Day 6) post morning dose of Day 5
for immunogenicity: pre morning dose on Day 1 and on Day 12 ± 1 post dose of Day 1

Spirometry: pre morning dose and 0.25, 0.5, 1, 2, 6, 10, 12 (=pre second dose) and 0.25, 0.5, 1, 2 and 4 h post second dose on Day 1 and pre morning dose and 0.25, 0.5, 1, 2, 6, 10, 12 (=pre second dose) and 0.25, 0.5, 1, 2 and 4 h post second dose on Days 2-5 and 24, 36, 48, 60 and 72 h post morning dose on Day 5

DLCO: 10 h post morning dose on Day 1 and pre morning dose on Days 2-4 and pre morning dose and 2 h post second dose on Day 5 and 72 h post morning dose on Day 5 (=Day 8)

Exhaled NO: pre morning dose on Days 2-5 and 24, 48, 72, 96 and 120 h post morning dose on Day 5

Safety assessments:
adverse events: throughout the study;
physical examination: 72 h (= Day 8) post dose on Day 5;
lung auscultation: pre morning dose and 0.25, 1, 12 (= pre second dose) and 0.25 and 1 h post second dose on Day 1 and pre morning dose and 0.25, 1, 12 (= pre second dose) and 0.25 and 1 h post second dose on Days 2-4 and pre morning dose and 0.25, 1, 12 (= pre second dose) and 0.25 and 1 h post second dose on Day 5 and 24 and 48 h post dose on Day 5;
vital signs: pre morning dose and 0.5, 1, 12 (= pre second dose) and 0.5, 1 and 4 h post second dose on Days 1-5;
12-lead ECG: pre morning dose and 12 (= pre second dose) and 2 and 4 h post second dose on Day 1 and pre morning dose and 4 h post second dose on Days 2-4 and pre morning dose and 1, 3, 6, 12 (= pre second dose) and 4 h post second dose on Day 5 and 24, 48 and 72 h post morning dose on Day 5;
clinical chemistry: pre morning dose on Days 2-5 and 24 and 72 h post morning dose on Day 5;
limited safety lab: 12 h post morning dose (= pre second dose) on Days 1-5;
exploratory safety lab: pre morning dose and 12 h (= pre second dose) on Day 1 and pre morning dose on Days 2-5 and 24, 48 and 72 h post morning dose on Day 5

Bioanalysis: analysis of plasma ALX-0171 samples using a validated method by sponsor

Intervention

Study Medication
Active substance: ALX-0171
Activity: Inhibition of the fusion (F) protein of hRSV

Indication: treatment of human respiratory syncytial virus (hRSV) infection
Strength: 50 mg/ml
Dosage form: nebuliser solution

Treatment(s)
SAD
Cohort 1: a single dose of 2.1 mg/ subject ALX-0171 or placebo on Day 1
Cohort 2: a single dose of 7 mg/ subject ALX-0171 or placebo on Day 1
Cohort 3: a single dose of 21 mg/ subject ALX-0171 or placebo on Day 1
Cohort 4: a single dose of 70 mg/ subject ALX-0171 or placebo on Day 1
Cohort 5: a single dose of 140 mg/ subject ALX-0171 or placebo on Day 1
Cohort 6: a single dose of 210 mg/ subject ALX-0171 or placebo on Day 1

MAD
Cohort 7: a single dose of X mg/ subject ALX-0171 or placebo twice daily on Days 1-5

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibility of an infetcion
Lungfunction tests: short of breath

See E9

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Healthy male volunteers
- Age between 18 - 55 years
- BMI between 18.0 - 30.0 kg/m2
- Only non-smokers

Exclusion criteria

Suffering from: Hepatitis B or C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 90 days from the start of the study of in case of donating more than 1.5 liter of blood in the 10 months prior the start of this study.

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:	Recruitment stopped
Start date (anticipated):	16-11-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	27-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-11-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-12-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-01-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-03-2012
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	EUCTR2011-001961-41-NL
CCMO	NL38441.056.11