A phase I, single-centre, randomised, single-blinded, placebo-controlled single ascending dose study, followed by an open-label extension, evaluating the safety, pharmacokinetics, pharmacodynamics and efficacy of ALX 0651, administered intravenously to healthy male volunteers.

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The objectives of this study are to:* To establish the safety and tolerability of ALX 0651, administered i.v. to healthy volunteers.* To investigate the pharmacokinetics of ALX 0651, administered i.v. to healthy volunteers.* To investigate the...

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

Summary

ID

NL-OMON35929

Source
ToetsingOnline

Brief title
ALX 0651 SAD and open-label extension in healthy male

Condition

- Other condition

Synonym
beenmerg, bloedvormende stamcellen

Health condition

stamcel mobilisatie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ALX 0651, blood forming stem cells, Bone marrow

Outcome measures

Primary outcome

safety and tolerability

pharmacokinetics

pharmacodynamics

biologically effective dose (BED) and/or maximum tolerated dose (MTD)

potential immunogenicity

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. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body (this is

called pharmacokinetics). In addition, the effect of the compound on the body will be investigated (this is called pharmacodynamics).
This study is not intended to improve your health, but is necessary for the further development of the compound.

Study objective

The objectives of this study are to:
* To establish the safety and tolerability of ALX 0651, administered i.v. to healthy volunteers.
* To investigate the pharmacokinetics of ALX 0651, administered i.v. to healthy volunteers.
* To investigate the pharmacodynamics of ALX 0651, administered i.v. to healthy volunteers.
* To establish one or more biologically effective dose (BED) levels and/or the maximum tolerated dose (MTD) of ALX 0651, administered i.v. to healthy volunteers.
* To investigate the potential immunogenicity of ALX 0651, administered i.v. to healthy volunteers.

Study design

Design:
a randomized, single-blinded, placebo-controlled, single ascending dose study with up to 8 cohorts with a maximum of twelve healthy male subjects per cohort each receiving a single intravenous dose of ALX 0651 or placebo; for the first and the second cohort sentinel staggering will be applied, two subjects (one active and one placebo) will be dosed and monitored for 24 h on Day 1 before the remaining subjects will be dosed; throughout the SAD part of the study one or more BED levels are likely to be established; the SAD will be followed by a open-label, single- or multiple-dose extension with up to two cohorts of twelve subjects receiving intravenous dose(s) of ALX 0651;

in the SD-OLE the (at most two) level(s) * 3 mg/kg that induced the highest CD34+ count in the SAD part of the study, without significant toxicity, will be explored, after administration of ALX-0651 at the respective BED level and determination of WBC count, (at most) 6 subjects that showed a sufficient pharmacodynamic effect (i.e., WBC * 30 x 109/L) will be assigned to receive aphaeresis;

when the BED is only established at the 6 mg/kg dose, or could not be established at all, the MD-OLE will be performed instead of the SD-OLE; In the MD-OLE ALX 0651 will be administered once-daily for a maximum of 3 consecutive days, depending on the safety and pharmacodynamic results obtained, the one or two dose levels * 3 mg/kg that yielded the highest CD34+ count in the SAD part of the study will be explored, each including 12 subjects, aphaeresis will be

performed in (at most) 2 x 6 subjects achieving * 20 CD34+ cells/µL following the first or second administration of ALX 0651

SAD and Single dose open label extension, subjects without aphaeresis:
Procedures and assessments:
-Screening and follow-up: clinical laboratory, physical examination, immunogenicity;12-lead ECG, vital signs; at eligibility screening: medical history, alcohol breath test and drug screen, HBsAg, anti HCV, anti-HIV 1/2, weight and height, abdominal ultrasound, clinical laboratory, physical examination, body weight and alcohol breath test to be repeated upon admission;

-Observation period:
one period in clinic from -17 h up to 48 h after drug administration and an ambulant visit on Day 14

- Blood sampling:
for pharmacokinetics of ALX-0651: pre-dose and at end of dosing and 0.5, 2, 4, 6, 10, 24, 30 and 48 h post-dose;
for immunogenicity (anti-ALX-0651 antibodies): pre-dose and 312 h post-dose
for flow cytometric analysis (CD34+ cell count): pre-dose and 1, 3, 6, 10, 24, 30, 48 and 312 h post-dose
for white blood cells count: pre-dose and 1, 2, 3, 6, 30 and 312 h post-dose
peripheral blood sample for clonogenic assay (GM-CFC, BFU-E, Mix-CFC): pre-dose and 1, 3, 6, 10 and 24 h post-dose

-Safety assessments:adverse events: throughout the study; physical exam: 48 h post-dose; vital signs: pre-dose and at end of dosing, 2, 6, 10, 24 and 48 h post-dose; 12-lead ECG: pre-dose and 24 and 48 h post-dose; clinical laboratory (haematology and chemistry): 10, 24 and 48 h post-dose

Single dose open label extension, subjects receiving aphaeresis:
Procedures and assessments
-Screening and follow-up:clinical laboratory, physical examination, immunogenicity;12-lead ECG, vital signs; at eligibility screening: medical history, alcohol breath test and drug screen, HBsAg, anti HCV, anti-HIV 1/2, weight and height, abdominal ultrasound, clinical laboratory, physical examination, body weight and alcohol breath test to be repeated upon admission

-Observation period:
one period in clinic from -17 h up to 48 h after drug administration and an ambulant visit on Day 14

- Blood sampling:
for pharmacokinetics of ALX-0651: pre-dose and at end of dosing and 0.5, 2, 24 and 48 h post-dose;

for immunogenicity (anti-ALX-0651 antibodies): pre-dose and 312 h post-dose
for flow cytometric analysis (CD34+ cell count): pre-dose and 1 h post-dose
for white blood cells count: *pre-dose and 1, 2 and 312 h post-dose
peripheral blood sample for clonogenic assay (GM-CFC, BFU-E, Mix-CFC): pre-dose and 1 h post-dose
for aphaeresis: 3 h post-dose

-Safety assessments: adverse events: throughout the study; physical exam: 24 and 48 h post-dose; vital signs: pre-dose and at end of dosing, 2, 10, 24 and 48 h post-dose; 12-lead ECG: pre-dose and 24 and 48 h post-dose; clinical laboratory (haematology and chemistry): 10, 24 and 48 h post-dose

Multiple dose open label extension, subjects receiving aphaeresis on Day 2: Procedures and assessments
-Screening and follow-up:clinical laboratory, physical examination, immunogenicity, 12-lead ECG, vital signs; at eligibility screening: medical history, alcohol breath test and drug screen, HBsAg, anti HCV, anti-HIV 1/2, weight and height, abdominal ultrasound, ; clinical laboratory, physical examination, body weight and alcohol breath test to be repeated upon admission

-Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 48 h after drug administration on Day 2 and an ambulant visit on Day 14

-Blood sampling:
for pharmacokinetics of ALX-0651: pre-dose and at end of dosing and 0.5, 2, 4, 6 and 10 h post-dose on Day 1, pre-dose and at end of dosing and 0.5, 2, 24 and 48 h post-dose on Day 2
for immunogenicity (anti-ALX-0651 antibodies): pre-dose on Day 1 and 288 h post-dose on Day 2
for flow cytometric analysis (CD34+ cell count): pre-dose and 1, 3, 6 and 10 on Day 1 and pre-dose and 1 h post-dose on Day 2
for white blood cells count: pre-dose and 1, 2, 3 and 6 h post-dose on Day 1 and 1, 2 and 288 h post-dose on Day 2
peripheral blood sample for clonogenic assay (GM-CFC, BFU-E, Mix-CFC): pre-dose and 1 h post-dose on Day 2
for aphaeresis: 3 h post-dose on Day 2

-Safety assessments: adverse events: throughout the study; physical exam: pre-dose, 24 and 48 h post-dose on Day 2; weight: pre-dose on Day 2; vital signs: pre-dose and at end of dosing, 2, 6, and 10 h post-dose on Day 1 and pre-dose, at end of dosing, 2, 10, 24 and 48 h post-dose on Day 2; 12-lead ECG: pre-dose on Day 1 and pre-dose and 24 and 48 h post-dose on Day 2; clinical laboratory (haematology and chemistry): 10 h post-dose on Day 1 and pre-dose, 10, 24 and 48 h post-dose on Day 2

Multiple dose open label extension, subjects receiving aphaeresis on Day 3
Procedures and assessments
-Screening and follow-up:clinical laboratory, physical examination, immunogenicity; 12-lead ECG, vital signs; at eligibility screening: medical history, alcohol breath test and drug screen, HBsAg, anti HCV, anti-HIV 1/2, weight and height, abdominal ultrasound, clinical laboratory, physical examination, body weight and alcohol breath test to be repeated upon admission;

-Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 48 h after drug administration on Day 3 and an ambulant visit on Day 14

-Blood sampling:
for pharmacokinetics of ALX-0651: pre-dose and at end of dosing and 0.5, 2, 4, 6 and 10 h post-dose on Day 1, pre-dose and at end of dosing at Day 2, pre-dose and at end of dosing and 0.5, 2, 24 and 48 h post-dose on Day 3
for immunogenicity (anti-ALX-0651 antibodies): pre-dose on Day 1 and 264 h post-dose on Day 3
for flow cytometric analysis (CD34+ cell count): pre-dose and 1, 3, 6 and 10 on Day 1 and pre-dose, 1, 3, 6 and 10 h post-dose on Day 2, pre-dose and 1 h post-dose on Day 3
for white blood cells count: pre-dose and 1, 2, 3 and 6 h post-dose on Day 1 and 1, 2, 3 and 6 h post-dose on Day 2, 1, 2 and 264 h post-dose on Day 3
peripheral blood sample for clonogenic assay (GM-CFC, BFU-E, Mix-CFC): pre-dose and 1, 3 and 6 h post-dose on Day 2
for aphaeresis: 3 h post-dose on Day 3

-Safety assessments: adverse events: throughout the study; physical exam: pre-dose on Day 2, pre-dose, 24 and 48 h post-dose on Day 3; weight: pre-dose on Days 2 and 3; vital signs: pre-dose and at end of dosing, 2, 6, and 10 h post-dose on Day 1 and pre-dose, at end of dosing, 2, 6 and 10 h post-dose on Day 2, pre-dose, at end of dosing, 2, 10, 24 and 48 h post-dose on Day 3; 12-lead ECG: pre-dose on Days 1 and 2 and pre-dose and 24 and 48 h post-dose on Day 3; clinical laboratory (haematology and chemistry): 10 h post-dose on Day 1 and pre-dose and 10 h post-dose on Day 2 and pre-dose,10, 24 and 48 h post-dose on Day 3

Multiple dose open label extension, without aphaeresis
Procedures and assessments
-Screening and follow-up:clinical laboratory, physical examination, immunogenicity 12-lead ECG, vital signs; at eligibility screening: medical history, alcohol breath test and drug screen, HBsAg, anti HCV, anti-HIV 1/2, weight and height, abdominal ultrasound ; clinical laboratory, physical examination, body weight and alcohol breath test to be repeated upon admission; at follow-up only: immunogenicity

-Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 48 h after drug administration on Day 3 and ambulant visit on Day 14

-Blood sampling:
for pharmacokinetics of ALX-0651: pre-dose and at end of dosing and 0.5, 2, 4, 6 and 10 h post-dose on Day 1, pre-dose and at end of dosing at Day 2, pre-dose and at end of dosing and 0.5, 2, 4, 6, 10, 24, 30 and 48 h post-dose on Day 3
for immunogenicity (anti-ALX-0651 antibodies): pre-dose on Day 1 and 264 h post-dose on Day 3
for flow cytometric analysis (CD34+ cell count): pre-dose and 1, 3, 6 and 10 on Day 1 and pre-dose, 1, 3, 6 and 10 h post-dose on Day 2, pre-dose and 1, 3, 6, 10, 24, 30, 48 and 264 h post-dose on Day 3
for white blood cells count: pre-dose and 1, 2, 3 and 6 h post-dose on Day 1 and 1, 2, 3 and 6 h post-dose on Day 2, 1, 2, 3, 6, 30 and 264 h post-dose on Day 3
peripheral blood sample for clonogenic assay (GM-CFC, BFU-E, Mix-CFC): pre-dose, 1, 3 and 6 h post-dose on Day 2

-Safety assessments: adverse events: throughout the study; physical exam: pre-dose on Day 2, pre-dose and 48 h post-dose on Day 3; weight: pre-dose on Days 2 and 3; vital signs: pre-dose and at end of dosing, 2, 6, and 10 h post-dose on Day 1 and pre-dose, at end of dosing, 2, 6 and 10 h post-dose on Day 2, pre-dose, at end of dosing, 2, 10, 24 and 48 h post-dose on Day 3; 12-lead ECG: pre-dose on Days 1 and 2 and pre-dose and 24 and 48 h post-dose on Day 3; clinical laboratory (haematology and chemistry): 10 h post-dose on Day 1 and pre-dose and 10 h post-dose on Day 2 and pre-dose,10, 24 and 48 h post-dose on Day 3

Bioanalysis:
-analysis of plasma ALX-0651 samples using a validated method by sponsor
-flow cytometric analysis (CD34+ cell count) using a validated method by PRA
-clonogenic assays using a validated method by sponsor
-analysis of anti-ALX-0651 antibodies samples using a validated method by sponsor

Intervention

ALX-0651 as bolus injection for first dose level, rest by iv

Study burden and risks

procedures: pain, light bleeding, heamatoma, possibility an infection.
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 volunteer
- Age between 18-55 years
- BMI between 19-29 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 or 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:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-06-2011
Enrollment:	76
Type:	Actual

Ethics review

Approved WMO Date:	30-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	24-06-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-11-2011
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	EUCTR2011-001135-23-NL
CCMO	NL36986.056.11