Double-blind, placebo-controlled, multiple ascending-dose study to investigate the safety and tolerability of AZ01 in healthy volunteers.

Published: 27-11-2009
Last updated: 10-08-2024

Primary:- assess safety and tolerability and determine the maximum tolerated dose (MTD) of repeated doses or a single dose of AZ01 given as a subcutaneous (SC) or intravenous (IV) dose in healthy subjects. Dosing will not exceed the maximum feasible...

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

Summary

ID

NL-OMON36500

Source
ToetsingOnline

Brief title
AZ01 (PEGYLATED INTERFERON BETA)

Condition

- Autoimmune disorders

Synonym
Multiple Sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Allozyne, Inc.

Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: AZ01, Multiple Sclerosis, Pegylated interferon Beta

Outcome measures

Primary outcome

Pharmacokinetics:

Plasma AZ01 concentrations, pharmacokinetic parameters.

Safety:

Adverse events, vital signs, ECG-parameters, laboratory parameters, physical

examination, TSH and antibodies to AZ01.

Pharmacodynamics:

Plasma markers (neopterin), quantitative gene expression (MxA and OAS).

Secondary outcome

N/A

Study description

Background summary

The drug to be given, AZ01, is a new, investigational compound that may eventually be used for the treatment of Multiple Sclerosis. Multiple Sclerosis is a disease of suspected autoimmune cause, in which the body's immune response attacks a person's central nervous system (brain and spinal cord), affecting the ability of nerve cells in the brain and spinal cord to communicate with each other.
Interferon-beta (IFN-beta) has been established as standard of care in the treatment of Multiple Sclerosis. IFN-beta is an endogenous compound involved in

inflammation processes. Though the currently available IFN-beta products provide significant benefit, its non-desirable effects (like flu-like illness, headache and fever) and the short activity requiring frequent injections (from 3 times weekly to weekly) may limit their utility. AZ01, a different form of INF-beta with an extended activity, was designed to address these issues.

Study objective

Primary:
- assess safety and tolerability and determine the maximum tolerated dose (MTD) of repeated doses or a single dose of AZ01 given as a subcutaneous (SC) or intravenous (IV) dose in healthy subjects. Dosing will not exceed the maximum feasible dose, determined for this study to be 10 mg.

Secondary:
- evaluate the pharmacokinetic (PK) profile of AZ01 with repeated doses or a single dose;
- evaluate biomarkers of AZ01 activity with repeated doses or a single dose of AZ01.

Study design

Design:
This is a single-center, double-blind, placebo-controlled study with 3 successive escalating cohorts, each containing 8 subjects each. Five additional cohorts were subsequently added to evaluate the safety, PK and PD of AZ01 that had been manufactured with improved purification processes. In Cohorts A through E, eight subjects will be randomly assigned at a 3:1 ratio (AZ01:placebo) to receive study drug at 14 day intervals for a total of 3 doses. Eight subjects in Cohort F will be randomly assigned at a 3:1 ratio (AZ01:placebo) to receive a three doses of study drug on Days 1, 19 and 43. Eight subjects in Cohort G will receive two doses of study drug on Days 1 and 15. Eight subjects in Cohort H will receive one intravenous dose of 0.5 mg study drug on Day 1. Eight subjects in Cohort I will receive one intravenous dose of maximum 3.0 mg study drug on Day 1.

Cohort G:
Procedures and assessments
Screening and follow-up:
Medical history, medication history, clinical laboratory, physical examination, ECG, vital signs (including blood pressure, pulse, oral temperature and respiratory rate), TSH and pregnancy test (females only); at eligibility screening: drug screen, anti-HBsAg, anti HCV, anti-HIV 1/2, weight, height and BMI; to be repeated upon first admission: physical examination, weight, ECG, vital signs (including blood pressure, pulse, oral temperature and respiratory rate), clinical laboratory, alcohol and drug screen, medical history,

medication history, and pregnancy test (females only); to be repeated upon each admission: urine drug screen; at follow up: AEs.

Observation period:
In clinic from -17 h up to 72 h after drug administration on Day 1 followed by ambulatory visits on Days 6, 8 and 11, in clinic from -17 h up to 24 h after drug administration on Day 15 followed by ambulatory visits on Day 20, 22, 25, 29, 32, 36 and 40; follow-up on Day 43.

Blood sampling
Serum/plasma samples:
AZ01 concentration: pre-dose on Days 1 and 15; post-dose at 6 and 12 hours on Days 1 and 15; at 24 hours post-dose on Days 2, and 16; at 36 hours post-dose on Days 2 and 16; and once on Days 3, 4, 6, 8, 11, 17, 18, 20, 22, 25, 29, 32, 36, 40, and 43.
Antibodies to AZ01: pre-dose on Days 1 and 15; and on Day 43; subjects with measurable antibodies at Day 43 will be asked to be tested approximately every 3 months until either test is negative or 12 months after last dose.
Biomarker analysis: pre-dose on Days 1and 15; post-dose at 12 hours on Days 1and 15; at 24 hours post-dose on Days 2, and 16; at 36 hours post-dose on Days 2 and 16; and once on Days 3, 4, 6, 8, 11, 17, 18, 20, 22, 25, 29, 32, 36, 40, and 43.
Whole blood samples:
Biomarker analysis: pre-dose on Days 1and 15; post-dose at 12 hours on Days 1and 15; at 24 hours post-dose on Days 2, and 16; at 36 hours post-dose on Days 2 and 16; and once on Days 3, 4, 6, 8, 11, 17, 18, 20, 22, 25, 29, 32, 36, 40, and 43.

Safety assessments:
Medical and medication history: Complete review at Screening. Interim review at Check-in; pre-dose Days 1 and 15; Days 2 and 16 (at 24 h post-dose); and in addition once on Days 3, 4, 8, 17, 18, 22, 29, and 43.

Physical examination: Screening, Check-In, Day 15 (pre-dose) and Day 43 (follow-up).

12-lead ECG: Screening; Check-in; Day 15 (pre-dose); Days 3 and 17 (48 hours post-dose); Day 43 (follow-up).

Vital signs: Screening; Check-in; Days 1 and 15 (pre-dose; and 2, 6, and 12 hours post-dose); Days 2 and 16 (24 and 36 hours post-dose); Days 3, 4, 17, and 18 (prior to discharge); and Days 8, 22, 29, and 43 (follow-up).

Adverse events:Days 1 and 15 (pre-dose; and 2, 6, and 12 hours post-dose); Days 2 and 16 (24 and 36 hours post-dose); Days 3, 4, 17, and 18 (prior to discharge); and Days 8, 22, 29, and 43 (follow-up).

Bioanalysis:
- analysis of plasma AZ01 samples using a validated method by Sponsor
- analysis of antibodies to AZ01 samples using a validated method by Sponsor
- biomarker analysis using a validated method by Sponsor

Cohort H and I:
Procedures and assessments
Screening and follow-up:
Medical history, medication history, clinical laboratory, physical examination, ECG, vital signs (including blood pressure, pulse, oral temperature and respiratory rate), TSH and pregnancy test (females only); at eligibility screening: drug screen, anti-HBsAg, anti HCV, anti-HIV 1/2, weight, height and BMI; to be repeated upon first admission: physical examination, weight, ECG, vital signs (including blood pressure, pulse, oral temperature and respiratory rate), clinical laboratory, alcohol and drug screen, medical history, medication history, and pregnancy test (females only); to be repeated upon each admission: urine drug screen; at follow up: AEs.

Observation period:
In clinic from -17 h up to 72 h after drug administration on Day 1 followed by ambulatory visit on Days 6, 8, 11, 15, 18, 22 and follow-up on Day 29.

Blood sampling
Serum/plasma samples:
AZ01 concentration: pre-dose on Day 1; post-dose at 6 and 12 hours on Day 1; at 24 hours post-dose on Day 2 at 36 hours post-dose on Day 2; and once on Days 3, 4, 6, 8, 11, 15, 18, 22, and 29.
Antibodies to AZ01: pre-dose on Day 1; Day 8; Day 15; Day 22; and on Day 29; subjects with measurable antibodies at Day 29 will be asked to be tested approximately every 3 months until either test is negative or 12 months after last dose.
Biomarker analysis: pre-dose on Day 1; post-dose at 12 hours on Day 1; at 24 hours post-dose on Day 2; at 36 hours post-dose on Day 2; and once on Days 3, 4, 6, 8, 11, 15, 18, 22, and 29.

Whole blood samples:
Biomarker analysis: pre-dose on Day 1; post-dose at 12 hours on Day 1; at 24 hours post-dose on Day 2; at 36 hours post-dose on Day 2; and once on Days 3, 4, 6, 8, 11, 15, 18, 22, and 29.

Safety assessments:
Medical and medication history: Complete review at Screening. Interim review at Check-in; pre-dose Day 1; Day 2 (at 24 h post-dose); and in addition once on Days 3, 4, 8, 15, 22, and 29.

Physical examination: Screening, Check-In, and Day 29 (follow-up).

12-lead ECG: Screening; Check-in; Day 3 (48 hours post-dose); Day 29 (follow-up).

Vital signs: Screening; Check-in; Day 1 (pre-dose; and 2, 6, and 12 hours post-dose); Day 2 (24 and 36 hours post-dose); Days 3 and 4, (prior to discharge); and Days 8, 15, 22, and 29 (follow-up).

Adverse events: Day 1 (pre-dose; and 2, 6, and 12 hours post-dose); Day 2 (24 and 36 hours post-dose); Days 3 and 4 (prior to discharge); and Days 8, 15, 22, and 29 (follow-up).

Bioanalysis:
- analysis of plasma AZ01 samples using a validated method by Sponsor
- analysis of antibodies to AZ01 samples using a validated method by Sponsor
- biomarker analysis using a validated method by Sponsor

Intervention

Study Medication:
Active substance : AZ01
Activity : unknown
Indication : unknown
Strength : 1.5 mg/mL
Dosage form : SC injection

Treatments:
Cohort G: 7.5 mg dose of AZ01 manufactured with improved purification process administered as five SC injections of AZ01 or placebo on each dosing day (Days 1 and 15).
Cohort H: 0.5 mg dose of AZ01 manufactured with improved purification process administered as one IV dose on one dosing day (Day 1).
Cohort I: Maximum 3.0 mg dose of AZ01 manufactured with improved purification process administered as one IV dose on one dosing day (Day 1).

Study burden and risks

Light bleeding and possibly an infection may occur.

Contacts

Public
Allozyne, Inc.

1600 Fairview Avenue East, Suite 300
Seattle, Washington 98102
US
Scientific
Allozyne, Inc.

1600 Fairview Avenue East, Suite 300
Seattle, Washington 98102
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy men and women, 18 and 45 years of age, inclusive, BMI 18 and 30 kg/m2, max. 5 cigarettes smoking per day.

Exclusion criteria

Suffering from: hepatitis B, 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 60 days from the start of the study. In case of donating more than 1.5 liters of blood (for men) / more than 1.0 liters of blood (for women) 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):	04-01-2010
Enrollment:	72
Type:	Actual

Ethics review

Approved WMO Date:	27-11-2009
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-12-2009
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-12-2009
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2009
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2010
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-05-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-08-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-08-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	19-10-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-11-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-11-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-12-2011
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	EUCTR2009-017341-54-NL
CCMO	NL30624.056.09