A single center, randomized, double-blind, 3-arm parallel Phase I study to assess pharmacokinetics, safety and tolerability of MYL-1402O solution for intravenous infusion after 90 minute intravenous infusion at one dose level (equivalent weight-adjusted dose (1 mg/kg) compared to the EU and US marketed drug product (Avastin®) in healthy male volunteers.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON42579

Source
ToetsingOnline

Brief title
MYL-1402O equivalency study to EU and US marketed Avastin.

Condition

- Plasma cell neoplasms

Synonym
Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Mylan Pharmaceuticals
Source(s) of monetary or material Support: Farmaceutische Industrie.

Intervention

Keyword: Avastin, cancer, MYL-1402O

Outcome measures

Primary outcome

To investigate the comparability of the pharmacokinetics (PK) of Mylan*s MYL 1402O solution for intravenous (i.v.) infusion versus the US and EU marketed versions of Avastin® as well as comparing the US approved Avastin® to EU approved Avastin® following a single 1 mg/kg i.v. infusion over 90 minutes in healthy adult male volunteers.

Secondary outcome

To compare the safety, tolerability, and immunogenicity of Mylan*s MYL-1402O with those of US and EU approved Avastin® following a single 1 mg/kg i.v. infusion over 90 minutes in healthy adult male volunteers.

Study description

Background summary

Avastin® is a drug registered for the treatment of cancer. Avastin® is the brand name; the active substance is called bevacizumab. Bevacizumab is a humanised monoclonal antibody (a type of protein that is normally made by the immune system to help defend the body from infection and cancer). Therefore, bevacizumab can be called *a biological*. Bevacizumab binds selectively to a protein called human vascular endothelial growth factor (VEGF), which is found on the lining of blood and lymph vessels in the body. The VEGF protein causes blood vessels to grow within tumors, these blood vessels provide the tumor with nutrients and oxygen. Once bevacizumab is bound to VEGF, tumor growth is prevented by blocking the growth of the blood vessels which provide the nutrients and oxygen to the tumor.

MYL 1402O is a new investigational compound which is being developed as a copy of Avastin®. Currently, MYL-1402O is being administered to humans for the first time in another clinical study, which is being conducted in cancer patients.

In this study the volunteer will receive MYL-1402O, Avastin® EU formulation (licensed product in the European Union) or Avastin ® US formulation (licensed product in the United States of America).

Study objective

The purpose of the study is to assess the concentrations of bevacizumab in the blood at different times after the volunteers have been administered MYL-14020 or Avastin® . In addition, it will be investigated to what extent MYL-10420 is tolerated. For the purpose of the study the concentration of bevacizumab and the possible development of antibodies against bevacizumab in the blood will be investigated.

Study design

The actual study will consist of 1 period during which the volunteers will stay in the clinical research center in Zuidlaren for 10 days (9 nights) followed by a period of 76 days during which they will visit the clinical research center on 8 occasions (on Day 12, Day 15, Day 22, Day 29, Day 43, Day 57, Day 71 and Day 85).

During the study the volunteers will receive MYL 1402O, Avastin® EU, or Avastin ® US formulation after breakfast in the morning as a 25 mL intravenous infusion of 90 minutes. From the start of the infusion, they will be required to remain in a lying or half-lying position for at least 4 hours.

Intervention

A single dose of 1 milligram per kilogram bodyweight MYL 1402O or 1 mg/kg of one of the two registered Avastin® formulations as a 25 milliliter (mL)

intravenous infusion of 90 minutes.

Study burden and risks

Blood sampling, indwelling cannula: During this study less than 300 mL of blood will be drawn. An indwelling cannula will be used on Days 1 and 2 to sample blood. In addition, from pre study screening until post-study screening approximately 18 times blood samples will be drawn by direct puncture of the vein. The blood samples to assess the concentrations of bevacizumab will be drawn after the volunteers has rested for at least 15 minutes; this rest will be in a lying position before the draws from Day 1 to Day 9 and in a sitting position before the draws at the short visits and post study screening.

Intravenous administration: For the intravenous administration the volunteer will have an indwelling cannula inserted specifically for this purpose in addition to the indwelling cannula used for blood sampling on Day 1. Thus the volunteer will have a cannula inserted in both arms during dosing. The cannula for the intravenous infusion will be removed immediately after administration of the infusion.

Vital signs: Respiratory rate, blood pressure, pulse rate and body temperature will be measured regularly.

Heart trace (ECG): ECGs will be made regularly.

Infusion site local tolerance: The infusion site on the volununteers skin will be examined several times during the study using a special score list.

The overall risks of MYL 1402O administration are considered to be minimal, although some are unforeseeable as the testing of this drug is still at an early stage. Although MYL 1402O is currently being administered in a clinical study in cancer patients, results from that study are not available yet. With the dose used in this study no serious side effects are expected, but as all drugs may potentially cause side effects to some extent, the occurrence of known or other effects cannot be excluded. This means that there is a chance of minor side effects and a remote chance of something serious happening. It is expected that MYL 1402O, which strongly resembles Avastin®, will likely have the same side effects as Avastin®.

Avastin® has been a registered drug for 11 years now for the treatment of several types of cancer. The regular dose for cancer patients starts at 5 mg/kg. In this study the volunteer will receive a lower dose of 1 mg/kg. The side effects described below were seen when Avastin® was given in cancer patients who used the drug for a long time together with chemotherapy. In this study only healthy volunteers will be included, who will receive a single dose. Therefore it is thought that the probability of the side effects described below to happen in this study is very low.

The most common side effects with Avastin are hypertension (high blood pressure), fatigue, asthenia (weakness), feeling of numbness or tingling in hands or feet, nausea, vomiting, diarrhoea and abdominal pain. The most serious side effects are gastrointestinal perforation (hole in the gut), hemorrhage (bleeding) and arterial thromboembolism (blood clots in the arteries).

The body may recognize MYL 1402O and Avastin®, as foreign. As a result an immune response can occur, for example by making antibodies against the study compound. However, based on experience with Avastin®, the chance of this happening is considered very low. If the volunteer developes antibodies, this is not expected to have consequences for the volunteer present health, but possibly in the future.

The effects of MYL-1402O on sperm cells and a possible pregnancy are not known. The volunteers agree to take effective measures to prevent pregnancy in a female partner and not to donate sperm during the study and until 6 months after administration of the study compound. Adequate contraception for the volunteer and his fertile female partner is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm or cervical cap, or a condom. Also, total abstinence, in accordance with the volunteers lifestyle, is acceptable.

Contacts

Public
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US
Scientific
Mylan Pharmaceuticals

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male volunteers
18 - 55 years, inclusive
60 - 100 kilograms, inclusive
BMI 19.0 - 30.0 kilograms/meter2
Non smokers or Light smokers

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 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 in the 10 months prior the start of this study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2015
Enrollment:	111
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin® EU
Generic name:	Avastin® EU
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Avastin® US
Generic name:	Avastin® US
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-03-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-03-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-04-2015
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	EUCTR2014-005621-12-NL
CCMO	NL52531.056.15