An open label study to assess the safety and tolerability of PB006 administered as a single intravenous infusion

Published: 04-02-2019
Last updated: 10-01-2025

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Ethical review	Approved WMO
Status	Completed
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON48246

Source
ToetsingOnline

Brief title
PB006 single dose safety study

Condition

- Neuromuscular disorders

Synonym
Multiple Sclerosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: PB006, Safety

Outcome measures

Primary outcome

- safety

- tolerability

Secondary outcome

N/A

Study description

Background summary

The sponsor is developing PB006, a compound similar to Tysabri. In preparation for medical-scientific studies to confirm the similarity of the two compounds, the Sponsor wants to study the safety of PB006.

Tysabri is a drug approved in Europe and the USA for the treatment of Multiple Sclerosis (MS) and in the USA also for the treatment of Crohn*s Disease. MS causes inflammation in the brain that damages the nerve cells. Symptoms of MS can include: walking problems, numbness in the face, arms or legs, problems seeing things,
tiredness, feeling off-balance or light headed, bladder and bowel problems, difficulty in thinking and concentrating, depression, acute or chronic pain, sexual problems, stiffness, and muscle spasms.

The active ingredient of PB006 and Tysabri is natalizumab which is an antibody. These antibodies work by binding to proteins in the body so that the harmful effect of that protein is removed. Tysabri stops the cells that cause inflammation from going into the brain. This reduces nerve damage caused by MS.

Study objective

The purpose of this study is to investigate the safety and tolerability of the new compound PB006 (natalizumab) when it is administered to healthy volunteers. PB006 has not been administered to humans before. It has been previously tested in the laboratory and on animals. PB006 is a biosimilar to Tysabri®, this means

it contains the same active substance (natalizumab) as Tysabri, a drug marketed and used for the treatment of patients with Multiple Sclerosis (MS).

This study will be performed in 10 healthy male/female volunteers. The study will be performed in 1 part.

Study design

The study will consist of 1 period during which the volunteer will stay in the research center for 4 days (3 nights). This will be followed by 2 days during which you will visit the research center for a short visit. These short visits will take place on Day 7 and 14.

The volunteer will be given 300 mg PB006 as an intravenous infusion (solution of the compound that will be administered directly in a blood vessel), administered over 60 minutes.

For safety reasons, initially 2 volunteers will receive the study compound at least 2 hours apart. After administration, the safety and tolerability of the study compound in these 2 volunteers will be closely monitored. If there are no concerns about the safety and tolerability 48 hours after administration, then the remaining 8 volunteers will receive the study compound. The study will be discontinued if, in the opinion of the responsible doctor, unacceptable side effects appear.

Intervention

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Study burden and risks

As with any drug, the study compound may cause side effects, though not everybody will be affected.
As PB006 will be administered to man for the first time in this study, side effects of PB006 in man have not been reported to date. However, PB006 is highly similar to Tysabri (natalizumab) that has been marketed and given to

patients.
The following side effects are most frequently observed (in 1 in 10 people or more) in medical-research studies with Tysabri/natalizumab:

• Urinary tract infection
• Sore throat and runny or blocked up nose
• Shivering
• Itchy rash (hives)
• Headache
• Dizziness
• Feeling sick (nausea)
• Being sick (vomiting)
• Joint pain
• Fever
• Tiredness

Possible risk of development of progressive multifocal leukoencephalopathy (PML)

JCV is a common virus that is generally harmless to humans and often acquired during childhood. It does not cause symptoms in people whose immune system functions normally. However, JCV can cause PML in people with weakened immune systems. Causes of a weakened immune system may include HIV infection, leukemia or lymphoma, or taking a medication such as Tysabri. Testing positive for JCV antibodies means that a person has been exposed to JCV in the past.

If the volunteer has been treated with Tysabri or with an immunosuppressant medication or in case the volunteer should test positive for JCV, he/she will not be eligible to participate in this study. Therefore, all risk factors for PML will not be present in order to reduce the potential risk as much as possible.
PML is a rare disorder in which the coating (myelin) of brain nerve fibers gets damaged. The most prominent symptoms of PML are clumsiness, progressive weakness, visual changes, speech changes, and sometimes personality changes. PML can result in death or variable degrees of neurological disability. There are no cases of PML known in healthy volunteers without JCV antibodies, after administration of Tysabri.
In people testing negative for JCV, the incidence of PML is estimated at less than 1 in 10,000. However, people with all three known risk factors have a higher estimated risk of PML. The risk factors are:
• The presence of anti-JCV antibodies.
• Longer duration of Tysabri treatment, especially beyond 2 years.
• Prior treatment with an immunosuppressant medication (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, or mycophenolate mofetil).

Possible discomforts due to procedures

Drawing blood and/or insertion of the indwelling cannula (tube in an arm vein) may be painful or cause some bruising.
In total, we will take about 100 milliliters (mL) of blood from the volunteer. This amount does not cause any problems in adults.
To make a heart tracing, electrodes (small, plastic patches) will be pasted at specific locations on the arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Contacts

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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 males and females
- 18-65 years, inclusive
- BMI: 18.5-32.0 kg/m2

Exclusion criteria

1. Any known exposure to natalizumab, alemtuzumab, ocrelizumab, daclizumab, rituximab, ofatumumab or obinutuzumab or any other B- and T-cell targeting therapies.
2. Any known exposure to immunosuppressive agents (e.g. methotrexate, cyclosporine, azathioprine, mitoxantrone, tacrolimus)
3. Known or suspected hypersensitivity to natalizumab, or any components of the formulation used (L-histidine/L-histidine hydrochloride, sodium chloride, polysorbate 80).
4. Any exposure to steroids within one month prior to dosing, to agents such as interferon-β, glatiramer acetate, fingolimod laquinimod within the last 2 months, toteriflunomide during the last 3.5 months, or to dimethyl fumarate within 6 months prior to dosing.
5. Positive test for anti-JCV antibodies [screening 1].
6. Female subject who has been pregnant within 6 months prior to screening 2, or breastfeeding or lactating within 3 months prior to screening 2.
7. Any of the liver enzymes (AST, ALT, alkaline phosphatase [ALP], gamma-glutamyltransferase [GGT]) and TBL above the ULN. In such a case the assessment may be repeated once. [Screening 2 and Day-1]
8. Any clinically significant history of allergic conditions (including drug allergies, asthma, eczema, or anaphylactic reactions, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).;Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	04-03-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Natalizumab

Ethics review

Approved WMO Date:	04-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-02-2019
Application type:	First submission
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	EUCTR2018-004761-13-NL
CCMO	NL68917.056.19

Study results

Date completed:	08-05-2019
Results posted:	10-11-2021

First publication
07-11-2019