Randomized, single-dose, parallel-arm, open-label Phase I trial to compare the pharmacokinetics, safety and tolerability of BI 695501 administered subcutaneously via prefilled syringe or autoinjector

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

Summary

ID

NL-OMON42895

Source
ToetsingOnline

Brief title
Study comparing PK of BI 695501 between prefilled syringe and autoinjector

Condition

- Autoimmune disorders

Synonym
Rheumatoid arthritis

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: BI 695501, healthy volunteers

Outcome measures

Primary outcome

1. AUC0-1368 (area under the concentration-time curve of the analyte in plasma

over the time interval from 0 to 1368 hours after dose).

2. Cmax (maximum measured concentration of the analyte in plasma).

3. AUC0-* (area under the concentration-time curve of the analyte in plasma

over the time interval from 0 extrapolated to infinity).

Secondary outcome

Pharmacokinetics: Tmax, lambdaz, t1/2, CL/F, VZ/F.

Study description

Background summary

BI 695501 is being developed as an alternative to Humira®, a compound which is already approved as a drug for the treatment of several autoimmune diseases including rheumatoid arthritis, Crohn*s disease, ulcerative colitis, psoriasis, hidradenitis suppurativa (acne inversa), and non-infectious uveitis. Autoimmune diseases arise from an abnormal immune response of the body against substances and tissues normally present in the body. BI 695501 inhibits inflammatory reactions by binding to a certain protein in the body, which decreases the immune response. Specifically, BI 695501 interferes with the working of a cytokine involved in inflammation, called TNF-alpha. The active substance of Humira® is called *adalimumab*. The Sponsor has manufactured BI 695501 to be biologically similar to adalimumab (biosimilar). BI 695501 has already been

studied in the laboratory and given to animals and humans.

Study objective

The main purpose of this study is to compare the pharmacokinetic characteristics of BI 695501 after subcutaneous (under the skin) injection in the thigh using either a prefilled syringe or autoinjector (a medical device for injecting a drug). The pharmacokinetics of a compound looks at how the compound gets into the bloodstream, how it is distributed throughout the body, as well as the chemical changes the drug undergoes as it is broken down by the body. It also examines the effects of the break down products and how they are passed out of the body.

A second purpose of this study is to test how safe BI 695501 is and what (if any) side effects are observed when it is administered has been taken.

Finally, the formation of antibodies against BI 695501 will be investigated.

Study design

The study will consist of 1 period during which the volunteer will stay in the clinical research center for 9 days (8 nights). The volunteer will stay from the afternoon of Day -1 (1 day before administration of the study compound; also called admission) to the morning of Day 8. This will be followed by 6 days during which the volunteer will visit the clinical research center for a short ambulatory visit: Days 10, 15, 22, 29, 36 and 43.

At admission on Day -1, the volunteer is expected at the clinical research center at 14:00 h in the afternoon. The volunteer will be required not to have consumed any food or drinks during the 4 hours prior to admission (with the exception of water).

For each short ambulatory visit, the volunteer is expected at the clinical research center at 8:00 h in the morning. For the short ambulatory visit on Day 22, the volunteer will be required not to have consumed any food or drinks during the 4 hours prior to arrival in the clinical research center (with the exception of water). There are no food or fluid restrictions prior to arrival for the short ambulatory visits on Days 10, 15, 29, 36 and 43.

The participation to the entire study, from pre-study screening until the telephonic follow-up, will be approximately 100 days.

On Day 1 the volunteer will receive a single subcutaneous injection in the thigh of 40 mg BI 695501 in a 0.8 mL solution, either by a pre-filled syringe or by an autoinjector.

Intervention

The volunteer will receive one single subcutaneous injection in the thigh of 40 mg BI 695501 in a 0.8 milliliter (mL) solution. BI 695501 will be given either by a pre-filled syringe or by an autoinjector. With a pre-filled syringe the drug is delivered through a needle which is inserted manually into the skin. An autoinjector contains a pre-filled syringe with a needle which is automatically inserted by pressing the autoinjector against the skin.

Study burden and risks

Based on the laboratory results, testing in animals and humans, and the fact that BI 695501 is biologically similar to adalimumab, the side effects of BI 695501 are expected to be similar to those observed for adalimumab. BI 695501 acts by decreasing the activity of the immune system (part of the body which helps to protect against disease or other damaging foreign bodies). The expected side effects are related to the suppression of the immune system. To date, a total of 246 male healthy subjects received subcutaneous doses of 40 mg BI 695501 via a prefilled glass syringe in 2 trials. The dose of 40 mg BI 695501 was generally well tolerated. The most frequently reported AEs were headache and upper respiratory tract infections and mild injection site reactions.

Additionally, 614 patients with moderate to severe rheumatoid arthritis have been included and treated with BI 695501 or adalimumab in an ongoing clinical study. There have been no unexpected safety findings or clinically relevant safety concerns. The side effects observed so far are in line with the known safety profile of adalimumab.

Adalimumab is now marketed in the European Union and in USA for at least 10 years. The side effects documented for adalimumab and which are described below have been reported by patients with pre existing inflammatory diseases like rheumatoid arthritis and psoriasis who were treated with multiple doses of adalimumab and over longer time periods.

Because this study includes only healthy volunteers who will receive a single dose, the probability is considered low that any of the events described below will happen in this study.

The most common side effects (may affect more than 1 in 10 people) reported for adalimumab are:
* Injection site reactions (including pain, swelling, redness or itching)
* Respiratory tract infections (including cold, runny nose, sinus infection, pneumonia)
* Headache
* Abdominal pain

* Nausea and vomiting
* Rash
* Musculoskeletal pain.

Common side effects (may affect up to 1 in 10 people) for adalimumab reported in patients are:
* Adalimumab is a medicine that affects the immune system and can lower the ability of the immune system to fight infections or make any infection worse (including serious infections).
* Allergic reactions can happen with symptoms like hives, swelling of your face, eyes, lips or mouth, trouble with breathing.
* Nervous system problems with signs and symptoms that include: numbness or tingling of legs, arms and/or fingers, problems with your vision, weakness in your arms or legs, and dizziness, can occur.
* Blood dyscrasias (an imbalance of components of the blood) may occur in case the body does not make enough of the blood cells that help fight infections or help to stop bleeding. Symptoms can include fever that does not go away, bruising or bleeding very easily, or looking very pale.
* New heart failure or worsening of a pre-existing heart failure may occur with symptoms like shortness of breath, swelling of ankles or feet, sudden weight gain.
* Immune reactions have been reported and symptoms may include chest discomfort or pain that does not go away, shortness of breath, joint pain, or a rash on the cheeks or arms that gets worse in the sun.
* Liver problems can happen in people who use adalimumab. Possible symptoms are: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of the stomach (abdomen).
* Some people using adalimumab had new onset of psoriasis. Tell the responsible doctor if you develop red scaly patches or raised bumps that are filled with pus.
* In patients taking adalimumab on a long term basis, occurrence of cancer has been reported, e.g. skin cancer (generally not life-threatening if treated) or blood cancer and solid tumors (with a frequency of less than 1% of all patients).
Serious side effects that occurred less frequently with adalimumab are:
* Formulation of nodules on the organs (sarcoidosis)
* Stroke (cerebrovascular accident)
* Heart attack (myocardial infarction), irregular heartbeat (arrhythmia) or missing heartbeat(s) by inhibiting the impulse for the heartbeat (sinus arrest), swelling of the aorta - the main blood vessel that leads away from the heart, down through the abdomen to the rest of the body * (aortic aneurysm), blockage of the arteries (arterial occlusion)
* Blood clot in the lung (lung embolism), interstitial lung disease, scarring of the lungs (pulmonary fibrosis)
* Inflammation of the pancreas (pancreatitis), hole in the bowel (intestinal perforation).
* Kidney failure (renal impairment)

* Impotence (erectile dysfunction)

BI 695501 is a so-called *biological*; with respect to the properties of these drugs there is a chance that the body will develop antibodies against BI 695501 or that a hypersensitivity reaction will be induced. Based on experience with adalimumab, the chance that the volunteer will develop antibodies against BI 695501 is likely. Should the volunteer develop antibodies, this is not expected to have consequences for his or her health. However, in case the volunteer would develop a condition that could be treated with adalimumab in the future, it cannot be predicted whether and how these antibodies may influence the effect of treatment. Currently, the following conditions could be treated with adalimumab: rheumatoid arthritis, ankylosing spondylitis, axial spondyloarthritis, psoriatic arthritis, psoriasis, Crohn*s disease, and ulcerative colitis. In that case, your doctor will suggest the best possible treatment for the volunteer. As of today several medications are available for the treatment of the conditions mentioned above with a mode of action, efficacy and safety profile which is similar to adalimumab.

Overall the safety data of adalimumab show that it is considered a safe drug provided certain precautions are taken. It is expected that the same will be the case for BI 695501.

The needle cap on the prefilled syringe and autoinjector contains dry, natural rubber. In rare cases this may cause severe allergic reactions. However, since the injection will be performed by experienced study staff, the risk that this will happen is minimal. Also, volunteers with a known history of allergic reactions will not be included into the trial.

Procedures: possibility for pain, minor bleeding, bruising, possible infection.

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 male or female subjects
Aged between 18 and 65 years (inclusive)
BMI of >17.5 to <35.0 kg/m2

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. Blood donation of more than 500 mL within 30 days prior to administration of trial medication or intended donation during the trial. Chronic or relevant acute infections. Previous exposure to adalimumab or proposed adalimumab biosimilar drugs. Subjects with any immunological disorders or auto-immune disorders, (e.g., RA, lupus erythematosus, scleroderma, etc.).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-10-2016
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	11-10-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2016
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	EUCTR2016-003158-34-NL
CCMO	NL59366.056.16