WE WANT TO MAKE MANAGING NASH AND FIBROSIS EASIER

Information about the 1404-0043
clinical research study for NASH and fibrosis

Managing non-alcoholic steatohepatitis (NASH) and fibrosis currently relies entirely on lifestyle changes. Weight loss can be hard to achieve and maintain. That's why we're conducting this study – we want to find out whether an investigational medication could support weight loss and improve liver health in people with NASH and fibrosis.

We're looking for approximately 240 people to join the study, who, among other things:

- Are between 18 and 80 years old (inclusive)
- Have a diagnosis of NASH and fibrosis
- Have a BMI of 25 kg/m^2 or above and body weight of 70 kg or above

This brochure will explain how clinical research works in general, why this study is being carried out and what taking part would involve. If you still have questions after reading or would like to learn more, please do not hesitate to contact us – you'll find the details on the last page.

What is a clinical study?

A clinical study (also known as a clinical trial) is a carefully controlled scientific investigation that helps us answer questions about an investigational medication, such as:

- Is it safe?
- Does it work?
- Which dose works best?

Thousands of people all around the world take part in clinical studies every year. Without them, new treatments cannot be developed. The results of these studies must be approved by health authorities before a (inclusive) can be used by the general public. Every prescription and over-the-counter medication you have ever taken will have been investigated in clinical studies that were only possible because of their participants.

What will this study involve?

If you decide to take part, the study will last for up to 62 weeks (14.5 months), as outlined below:

Screening period - Up to 10 weeks

We'll carry out some tests to make sure that the study is right for you.

Double-blind treatment period - 48 weeks

You'll be assigned at random (like the flip of a coin) to one of four groups:

Group 1 will receive BI 456906. The dose will gradually increase from 0.3 mg to 2.4 mg and then remain at 2.4 mg per week from Visit 16 (Week 14)

Group 2 will receive BI 456906. The dose will gradually increase from 0.3 mg to 4.8 mg and then remain at 4.8 mg per week from Visit 20 (Week 18)

Group 3 will receive BI 456906. The dose will gradually increase from 0.3 mg to 6.0 mg and then remain at 6.0 mg per week from Visit 24

Group 4 will receive placebo during the entire treatment period

There's an equal chance of you being assigned to any of these four groups. Both the investigational medication and the placebo will be administered by subcutaneous injection (injection under the skin) once a week. Study staff will provide you with training so that you can do this at home between study centre visits.

Safety follow-up period - 4 weeks

We'll continue to monitor your health and condition.

What does the investigational medication do?

BI 456906 is a new type of medication that targets two receptors (proteins involved in regulating what goes on inside the cells).
This medication is expected to help reduce weight and lower the fat in your liver by:

- Reducing feelings of hunger and the need to eat
- Increasing your body's total energy expenditure and the breakdown of fat in your liver

What is a placebo?

A placebo is a substance that looks like the investigational medication but contains no active medication. It helps us to assess the effects of the investigational medication by giving us something to compare it to.

Will I know whether I am receiving the investigational medication or placebo?

This is a double-blind study, which means no one (including you and the study team) will know who is receiving the investigational medication or the placebo. This way, the results of the study will not be favoured one way or another because everyone will be cared for in the same way. But please be reassured that if it becomes necessary for your care, your study doctor will be able to find out whether you are taking the placebo or the investigational medication.

Will I experience side effects?

Some people may experience side effects of their assigned study medication, which can include nausea, vomiting and diarrhea. However, we'll do our best to help you manage any side effects through lifestyle advice, reducing the study medication dose or by offering certain medications.

How will my health be monitored?

During the study, you'll need to attend up to 34 study visits. This is so we can monitor your general health and see how you are responding to your assigned treatment. Visits will take place every week for the first 24 weeks, then every 4 weeks for the remainder of the treatment period. Approximately 60% of the study visits are anticipated to be conducted at the study site. The remaining study visits will be conducted remotely.

Health assessments will vary between visits, but may include:

Blood tests – these will be used to measure many different aspects of your health.

Urine samples – samples will be collected and analysed in a laboratory. These can tell us a lot about your overall health.

Physical examination – during the screening period you will have a physical examination during which we'll take a look at (among other things) your general appearance, skin and lungs. During the treatment period, a physical examination may be carried out if needed.

Electrocardiogram (ECG) – a painless test which measures the electrical activity of your heart.

Liver biopsy – a procedure where a small piece of tissue is removed from your liver with a needle. It is used to learn how severe your NASH is and how much scar tissue is present in your liver. It is typically performed under local anesthetic. You will need to fast (not eat or drink anything, except water) **overnight** before we take the liver biopsy. If you have recently had a liver biopsy, it may be possible that material from that biopsy can be used instead of performing a new biopsy at your screening visit.

Magnetic resonance imaging (MRI) – a test which uses a large magnet and radio waves, along with computer equipment, to produce pictures or images of the human body. To conduct this test, part or all of your body will be passed into a long, narrow tube scanner, which is open at both ends.

FibroScan® – a test which uses high-frequency sound waves to measure the stiffness of your liver and the amount of fat in your liver.

Questionnaires – you will be asked about your symptoms and quality of life. This helps us understand things like the impact you feel NASH and fibrosis are having on your daily life and the level of symptoms you are experiencing.

If you have diabetes we'll also ask you to test your blood glucose (sugar) levels at home so we can monitor your safety. To do this, you'll be given an electronic blood glucose meter (glucometer) to take home for the duration of the study. You may also use your own device. The study staff will show you how to get a blood sample from your finger, use the machine, and tell you when and how often you need to do the measurements. The study staff will also tell you what to do if your levels of blood glucose are too low or too high.

Frequently asked questions

Will I need to pay for anything?

No. If you take part, all study procedures including lab work, tests, doctor visits, and study medications and devices will be provided to you free of charge.

Can I choose whether or not to take part?

Yes. Your participation in this study is voluntary. If you join this study, you can stop at any time without any effect on your future healthcare options. We may simply ask that you attend a final visit so that we can help you leave the study in the safest way possible.

Can you guarantee my condition will improve?

No, we can make no guarantees about your health, unfortunately. Your condition might improve, but it could also remain the same or get worse during the course of this study. But please be reassured that you can contact the study team at any time if you are concerned.

How can I learn more?

If you have any questions or would like to find out more about the study, please contact the study team using the details below. They'll be happy to help.

Study team contact details: