Diabetes?
High cholesterol?
Obesity?

Having any of these conditions increases your risk for non-alcoholic steatohepatitis (NASH)

Non-alcoholic steatohepatitis (NASH) is a progressive liver disease where fat accumulates in the liver and causes inflammation and scarring in the liver (called fibrosis), which is visible under a microscope with a liver biopsy sample. If left untreated, the disease continues to progress and may lead to advanced fibrosis. NASH evolves from non-alcoholic fatty liver disease and can lead to liver cirrhosis, with a reduced life expectancy.[1] Once cirrhosis has developed, serious complications of liver disease may occur, including liver failure, liver cancer or even the need for a liver transplant.

NASH is the liver manifestation of metabolic disorders such as obesity, diabetes or high cholesterol. In addition, people with NASH have increased risks for cardiovascular complications, potentially leading to a heart attack or severe heart disease. Therefore, an ideal treatment for NASH should reduce the activity of the disease, resolve liver scarring and have a beneficial impact on metabolic and cardiovascular risks.

NASH is a global disease and the most common liver disorder in Western countries, affecting 14% of American adults.[2] Although NASH affects an increasing number of people, there are still no approved drug therapies for its treatment. Thus, clinical research, by conducting clinical trials, is essential to finding a potential treatment option for people with NASH.

The NATiV3 Trial is evaluating an investigational drug as a potential treatment for people living with NASH and fibrosis. If you are interested in learning about the NATiV3 Trial and curious to know if the trial may be an option for you, contact a member of our medical team. They will explain the details of the trial and answer all your questions.

Find out more about the trial in this brochure.

What is a clinical trial?

A clinical trial is carefully designed to look at the safety and effectiveness of potential new medical treatments. Trials are very controlled scientific evaluations of investigational drugs. Most treatments used today are the result of past clinical studies. Your participation in the NATiV3 Trial will help us understand whether the investigational drug may be a potential treatment for NASH.

Participation in this clinical trial is completely voluntary, and you can leave the trial at any time and for any reason. Your decision to participate or not participate in this clinical trial will have no effect on the medical care you receive now or in the future.

Like all medications, the investigational drug may cause side effects, although not everyone will experience them. You will be closely observed for any side effects throughout the clinical trial. Most side effects are mild to moderate; however, the possibility of serious side effects, which may require treatment, cannot be ruled out. You must immediately inform the study doctor if you have any adverse symptoms or if you notice any changes in your health during the trial.

Learn more about NATiV3

If you would like to learn more, please visit www.clinicaltrials.gov/ct2/show/NCT04849728 or www.nash-trial.com, or to schedule a visit to determine if you may be eligible to participate, please speak with a member of the study team.

[1] https://www.medicalnewstoday.com/articles/cirrhosis-of-the-liver-life-expectancy#life-expectancy-by-stage

[2] Harrison SA, et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. J Hepatol. 2021 Aug;75(2):284-291

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NATiV3 Trial – Patient Brochure – US – English – 11JAN2023 – Version 4.0

NASH

Working towards a potential treatment option

A clinical trial to evaluate an oral investigational drug in adults 18 years and older with NASH and liver fibrosis is now enrolling.

NATiV3
NASH LANIFIBRANOR PHASE 3 TRIAL

What is the NATiV3 Trial?

NATiV3 is a clinical trial for adults 18 years of age and older with NASH and liver fibrosis stage 2 or 3. The purpose of the trial is to evaluate if an oral investigational drug (lanifibranor) is a safe and effective potential treatment option for NASH. The clinical trial will evaluate if the investigational drug reduces the scars on your liver (fibrosis), resolves NASH, delays or stops damage to liver function and improves the way you feel throughout the trial.

About 1,000 people around the world who have NASH with fibrosis will participate in the NATiV3 Trial.

In addition, an exploratory cohort of approximately 200 patients who do not meet the main study criteria of NASH with F2/F3 liver fibrosis, but do have NASH or a high likelihood of NASH, will be evaluated.

What is the investigational drug?

The investigational drug in the NATiV3 Trial is called lanifibranor.

In the first part of this trial (Part A), the 2 different doses of the investigational drug will be compared to a placebo, which looks like the investigational drug tablet but contains no active ingredients. Participants will be assigned by chance to receive either 1 of the 2 doses of the investigational drug or placebo, meaning that participants have a 2-in-3 chance of receiving the investigational drug. Neither the participants nor the study staff will know whether each participant is receiving the investigational drug or placebo, but the study doctor can get this information if required for medical reasons. In the second part of the trial (Part B), participants will only receive lanifibranor.

Because there are no approved drugs available for NASH with fibrosis, participants assigned to receive the placebo in the first part of the trial will not be at an additional risk. All participants will receive standard-of-care treatment and will be closely monitored by the study team. If any new treatments are approved, your options will be explained to you by your study doctor.

NATiV3 Trial participation at-a-glance

If you choose to participate and are eligible, you will start the trial in **Part A** with a duration that can vary from 72 to 120 weeks for each individual participant, depending on when you start the trial. You will be taking either the **investigational drug or placebo** with a maximum of 10 on-site study visits. During the Week 72 visit, a liver biopsy will be **done for the main cohort only**.

You will be in **Part B** of the trial for 48 weeks and have 5 on-site visits. Every participant will receive the investigational drug lanifibranor for the potential treatment of NASH; no placebo will be given in this part. Even if you receive the placebo during Part A of the trial, you will receive lanifibranor (800 or 1200 mg/day) in Part B.

All people who join clinical trials are volunteers. We want you to make a choice based on your health and values. If you are offered a clinical trial, it is your right to decide whether to take part, and you can stop the trial at any time. Participation in the trial includes up to 35 visits with the study doctor, either at the trial site or by phone.

For more information about the investigational drug, tests or assessments, please speak with a member of the study team. They are here to help.

Screening

- Review trial and sign Informed Consent Form
- Review medical history and current prescriptions
- Lab tests
- Review of historical liver biopsy or perform a liver biopsy
- Review of eligibility criteria
- Review diet and lifestyle
- Conduct ECG
- Conduct elastography

Randomization into 1 of 3 groups

- Investigational drug (lanifibranor) 800 mg/day
- Investigational drug (lanifibranor) 1200 mg/day
- Placebo

Treatment Period Part A

Week 0 (Day 1) to Week 72 or maximum Week 120

- Take pills (lanifibranor/placebo) daily with your first meal of the day for 72 weeks (18 months) to a maximum of 120 weeks
- Attend a maximum of 10 on-site visits and 3 phone visits so the study doctor can check your health

Week 72 Visit

- Tests, questionnaires and a liver biopsy (main cohort only) to evaluate if there are changes in your liver tissue due to the investigational drug

Treatment Period Part B

Total of 48 weeks following Part A

- All participants will be taking lanifibranor (800 or 1200 mg/day)
- Continue to take pills (lanifibranor) daily with your first meal of the day
- Attend 5 on-site and 1 phone visit so the study doctor can check your health

End-of-study Visit

- After 48 weeks of treatment in Part B, you will stop the treatment, and there will be a final follow-up visit in approximately 4 weeks. This is the final planned study visit to evaluate safety.

Note: If you discontinue the trial early, you will be asked to attend a premature end-of-treatment visit. If this occurs during Part A, you will be asked to have a liver biopsy.
Note: The exploratory cohort undergoes the same assessments, except for the Week 72 liver biopsy, which will not be performed.

You may be able to participate in this clinical trial if you are 18 years of age or older and:

- Have been diagnosed with or are at risk for NASH with fibrosis
- Do not have any other chronic liver disease

There are other criteria that you must meet in order to participate in the NATiV3 Trial, which the study team can discuss with you.

Why should I participate in a clinical trial?

Participating in a trial is a way to learn more about your disease and how to take care of your health. As a participant, your NASH with fibrosis will be closely monitored under the guidance of the study doctor. Your participation in this trial may help bring a treatment for NASH to future patients.

All eligible trial participants will receive the following at no cost:

- The investigational drug or placebo in Part A, and the investigational drug lanifibranor only in Part B
- Trial-related visits, assessments and tests
- You may also be reimbursed for reasonable trial-related travel expenses