ChronicStatinMig

A multicenter, triple-blind, Placebo-Controlled, Parallel Study with atorvastatin for chronic migraine

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REQUEST FOR PARTICIPATION IN A CLINICAL TRIAL

Preventive Treatment with Cholesterol-Lowering Medication for Chronic Migraine

A Multicenter Triple-Blind Placebo-Controlled Parallel Study with Atorvastatin for Chronic Migraine

This is a request for your participation in a research project involving the testing of the medication atorvastatin. We are reaching out to you either because you have contacted us directly or because we have previously examined you. The purpose of the study is to investigate whether the cholesterol-lowering medication atorvastatin has a beneficial preventive effect on chronic migraine with acceptable side effects. Previously, three smaller studies conducted abroad suggest a potential beneficial effect on migraine with few side effects. Atorvastatin has been in use by many Norwegian patients for several decades. The study is conducted by St. Olavs Hospital and the Norwegian University of Science and Technology (NTNU), and takes place at five different hospitals in Norway.

WHAT DOES PARTICIPATION IN THE STUDY ENTAIL FOR YOU?

If you are between 18 and 64 years old, have chronic migraine, and are otherwise generally healthy, you may participate. Initially, you will be invited for a visit where the study physician will assess your suitability for the study. If you are pregnant or breastfeeding, you cannot participate, and if you are of childbearing age, you must use reliable contraception. Information gathered before inclusion will not be used as part of the study. If the study physician determines that you can participate, you must sign a declaration indicating your desire to participate in the study. You will have the opportunity for a reflection period if needed. The study will last a total of 21 weeks. After the first visit, you will keep a headache diary for one month and then return for another visit to the study physician. If you have fewer migraine days than desired, you may keep the headache diary for an additional month to see if your attack frequency is within the desired level. In that case, you will be provided with tablets for a 12-week treatment period. This will consist of either a moderate dose of cholesterol-lowering medication (40 mg) or placebo. Neither you, nor the doctor, nor the nurse will know which one you are receiving. A simple electronic headache diary must be maintained throughout the study period. After the 12 weeks, you will stop taking the medication but continue to fill the diary for an additional 4 weeks. Then, you will return for a final visit with the physician. The physician will then assess what the best migraine treatment for you would be. During the study, you may take acute migraine medication as needed, as you have done previously. There will also be follow-up telephone calls from a nurse during the study.

Blood samples will be taken from you before starting treatment and every 4 weeks during the treatment period to assess whether the medication affects bodily functions. You will receive requisitions for blood sample collection at the hospital or your nearest medical office. If you are a woman of childbearing age, you will undergo a pregnancy test both at inclusion, before starting treatment, and as a home test every month during treatment.

If you do not wish to participate or wish to withdraw from the study, you will be offered the treatment we usually provide based on your medical history (acute medication and possibly preventive medication), and you will be followed up by your regular doctor.

We use an electronic headache diary that is downloaded as an application on your smartphone. You will receive assistance in installing this. Therefore, please bring your smartphone for all visits. A

secure login is required the first time, and if you lack the "BankID app," you must also bring your "bank card" when you attend the first visit of the study. The mobile phone must be connected to the internet to securely store the diary on Microsoft Azure on a data server in Stavanger. If you are offline, the data will be temporarily stored on your phone and then transferred to Azure's server as soon as you are online.

There will be no commercial exploitation of you, your biological material, or your health information.

POTENTIAL BENEFITS AND RISKS

If you participate in the study, your migraine will be thoroughly mapped. You will have the opportunity to try out a potentially effective preventive medication with mostly minor side effects. After the study, you will receive an evaluation of the best treatment for you. Additionally, you will have contributed to research that may improve migraine treatment for patients worldwide. The disadvantage is that you will need to keep a headache diary for approximately 4 months, attend three doctor visits during this time, and undergo several blood tests throughout the study.

Atorvastatin is commonly used in patients with high cholesterol and is generally well tolerated. Side effects are usually mild. A few individuals may experience skin rash, gastrointestinal discomfort, and muscle pain. If you experience side effects or other health problems, it is important that you promptly inform the responsible study physician or the department you belong to. A rare but possible serious side effect is muscle inflammation, so it is important that you contact us promptly if you experience muscle pain.

VOLUNTARY PARTICIPATION AND POSSIBILITY TO WITHDRAW YOUR CONSENT

Participation in the study is voluntary. If you wish to participate, you sign the consent form on the last page. You may withdraw from the study at any time and for any reason without consequences for your further treatment.

If you agree to participate in the study, you have the right, under the EU General Data Protection Regulation (GDPR), to access the information recorded about you. You also have the right to have any inaccuracies in the information we have recorded corrected. You also have the right to access the security measures for processing the information. If you withdraw from the study, no further information or samples will be collected from you. Samples already collected and not yet analyzed will be destroyed. Information already collected will not be deleted and may be used in further research in this study. You can complain about the processing of your information to the Data Inspectorate and the institution's data protection officer.

If you later wish to withdraw or have questions about the study, you can contact the principal investigator responsible for the study at your hospital (see contact information below) or via the email address kontakt-hodepine@ntnu.no.

WHAT HAPPENS TO THE INFORMATION ABOUT YOU?

The information recorded about you will only be used as described in the purpose of the study. All information will be processed without names, national identification numbers, or other directly identifying information. A code will link you to your information through a name list kept together with your consent at each individual hospital. This means that the information recorded about you is de-identified. The list that can link your name to the code will only be kept in the electronic data

capture solution and at your nearest study hospital, and only the principal investigator and other physicians and study nurses associated with the study will have access to this list.

The information collected about you in the study will be used within the study until December 31, 2031, for when research activities including analysis and publication should be completed. The information will be stored for 25 years for control purposes after the last included patient has completed the study. Representatives from the sponsor, the Norwegian Medicines Agency, and regulatory authorities in Norway and abroad may be provided with study information and given access to relevant parts of your medical record. The purpose is to verify that the study information corresponds to the corresponding information in your medical record. Everyone who has access to information about you is bound by confidentiality. All data collected about you will be deleted on December 31, 2053.

Publication of results is an essential part of the research process and is done on aggregated data so that it is unlikely that you will be recognizable. Any extensions in the use and storage period can only occur after approval from the Regional Ethics Committee (REK) and other relevant authorities. There are no plans in this study to transfer collected information about you to other countries.

WHAT HAPPENS TO THE SAMPLES TAKEN FROM YOU?

At the start of the study and during the treatment phase, you will undergo blood tests to assess your blood sugar, as well as your muscle-, liver- and kidney function. Your LDL-cholesterol will also be measured at the first visit. These samples will be analyzed and interpreted promptly at your nearest university hospital participating in the study, either at St. Olavs Hospital, Akershus University Hospital, Haukeland University Hospital, Oslo University Hospital, or the University Hospital of Northern Norway. These blood samples will be destroyed immediately after analysis. If you experience muscle-related side effects, you might need to take another blood sample (HMGCR-antibodies) that will be sent to Oslo University Hospital.

APPROVALS

The Regional Committee for Medical and Health Research Ethics, Committee for Clinical Trials of Medicines and Medical Equipment (REK KULMU), has reviewed the study [2022-502176-23-01] and provided preliminary approval. We process information based on the EU General Data Protection Regulation Article 6(1)(e) and (3) and Article 9(2)(j) and (d), and your consent. You have the right to complain about the processing of your information to the Data Inspectorate.

CONTACT INFORMATION

St. Olavs Hospital and Principal Investigator Lise Rystad Øie is responsible for the privacy of the study

If you have questions about the study or wish to withdraw from participation, you can contact:

Lise Rystad Øie, St. Olavs Hospital: lise.r.oie@ntnu.no
Marte Bjørk, Haukeland Universitetssykehus: marte.bjork@uib.no
Kjersti Grøtta Vetvik, Akershus Universitetssykehus: Kjersti.Grotta.Vetvik2@ahus.no
Bendik Slagsvold Winsvold, Ullevål, Oslo Universitetssykehus: uxwinb@ous-hf.no
Linn Hofsøy Steffensen, Universitetssykehuset Nord-Norge: Linn.Hofsoy.Steffensen@unn.no
If you have questions about privacy in the study, you can contact the data protection officer at the principal investigator's institution: personvernombudet@stolav.no

Additional information about the study can be found in Chapter A - Detailed Explanation of the Study's Implications.

Additional information about biobanking, privacy, finance, and insurance can be found in Chapter B - Privacy, Biobank, Finance, and Insurance.

The consent form follows Chapter B and should be signed by the participant. The person who has provided information about the study can confirm that the information has been provided.

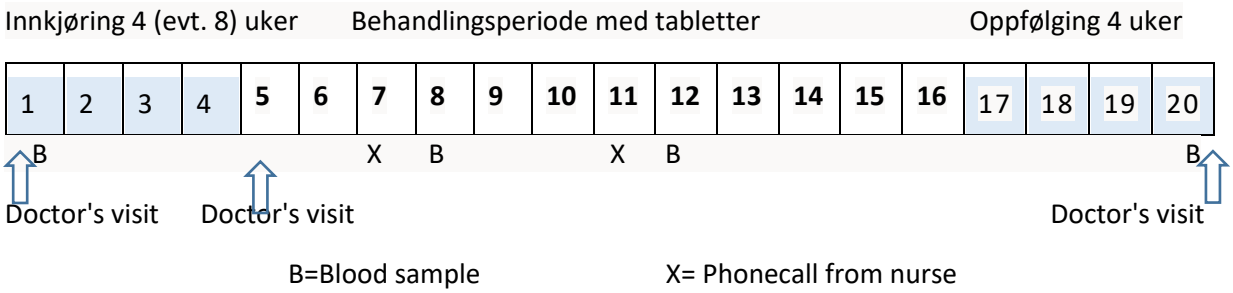
CHAPTER A – DETAILED EXPLANATION OF THE STUDY'S IMPLICATIONS

No data will be recorded for you if you cannot participate in the study, and information from the initial conversation with you will not be included as data in the study. After you have consented to participation, blood samples will be taken to check, among other things, liver, kidney, and muscle function. After this, you will receive instructions for uploading a migraine diary to be kept daily for 4 weeks. The physician will then meet with you again to assess your attack frequency and blood tests in relation to whether you can receive study medication. If there have been too few attacks, you may be asked to keep the diary for an additional 4 weeks. Atorvastatin has been used in the treatment of more than one million people worldwide and can be taken with most types of medications. If you need to start new medications during the study, you should discuss this with the study physician. The medication can be taken regardless of meals and with all types of foods. It is important that the medication is taken every day, preferably at about the same time each day.

The safety of using Atorvastatin during pregnancy has not been established, and if you are a woman of childbearing age, you must therefore use adequate contraception throughout the study. If you still become pregnant, you must discontinue the study, and you will be informed of the medication you have received.

A total of 300 patients with chronic migraine are planned to be included in the study.

S T U D Y P L A N



CHAPTER B - PRIVACY, BIOBANK, FINANCE, AND INSURANCE

WHAT INFORMATION ABOUT YOU IS COLLECTED?

Among the information recorded about you are headache frequency, age, gender, duration of education, blood pressure, pulse, other illnesses and other planned treatment, use of contraception, as well as past and current use of medications and dietary supplements. As part of clinical practice, the results of blood tests will be checked through your patient record, but these will not be collected as part of the study.

Representatives from the sponsor, the Norwegian Medicines Agency, and regulatory authorities in Norway and abroad may be provided with study information and given access to relevant parts of your medical record. The purpose is to verify that the study information corresponds to the corresponding information in your medical record. Everyone who has access to information about you is bound by confidentiality.

FINANCING

The initiative for this study comes from the Norwegian Centre for Headache Research, NorHead, which is a clinical treatment center funded by the Research Council of Norway. None of those responsible for the study receive additional remuneration for conducting the study.

FINANCE

Study medication, doctor's visits, and blood tests are provided free of charge. No extra fees will be paid in the study, but any expenses for blood sample collection at medical offices will be reimbursed.

INSURANCE

You are insured in accordance with the Product Liability Act in the Medicines Insurance and the Compensation Act for Patient Injuries.

INFORMATION ABOUT THE OUTCOME OF THE STUDY

You have the right to receive information about the outcome of the study. When the entire study is completed, you will be informed by letter about which medication you received.

Regardless of the outcome of the study, a summary of the study results tailored to the public will be made available through the EU portal Clinical Trials Information System (CTIS) within one year after the end of the study.

I CONSENT TO PARTICIPATE IN THE STUDY AND TO THE USE OF MY PERSONAL INFORMATION AND BIOLOGICAL MATERIAL AS DESCRIBED

With this, I also confirm that I have been informed about the study, that any questions have been answered, and that I have received a copy of the information sheet.

Place and date	Participant's signature
	Participant's name in capital letters

CONFIRMATION THAT INFORMATION HAS BEEN PROVIDED TO THE PARTICIPANT IN THE STUDY

I confirm that I have provided information about the study.

Place and date	Signature
Role in the study	Academic qualification