UCSF University of California San Francisco
IRB NUMBER: 17-21905
IRB APPROVAL DATE: 01/18/2022
IRB EXPIRATION DATE: 01/17/2023

TUFTS MEDICAL CENTER
TUFTS UNIVERSITY
Jean Mayer Human Nutrition Research Center on Aging

INFORMED CONSENT TO PARTICIPATE IN SCREENING

The Effect of SLC19A3 Inhibition on the Pharmacokinetics of Thiamine

Principal Investigator: Dr. Andrew Greenberg
Co-Investigators:

Study Physician: Lisa Ceglia, MD

Metabolic Research Unit (MRU): (617) 556-3042
Study Coordinator, Kim Vo Trinh: (617) 556-3220

Study Physician, Dr. Lisa Ceglia: (617) 556-3085, days

For emergencies at any time, including days, evenings, weekends and holidays, please call (617) 230-7545 to reach Dr. Ceglia, the study physician.

INTRODUCTION

You are being invited to screen for a research study at the Human Nutrition Research Center on Aging (HNRCA) at Tufts University evaluating the effect of drugs on vitamin B1 (thiamine) levels because you are a healthy individual between the ages of 18 and 65. Thiamine is an essential vitamin meaning you must consume thiamine in your diet in order stay healthy. Low thiamine levels can lead to adverse events.

If you continue with this screening, you will be asked to provide blood and urine samples, asked about your health history, and be asked to fill out a questionnaire to determine your eligibility. Your blood and urine samples will be used to evaluate your health status. Multiple tests will be performed including, but not limited to, a complete metabolic panel, pregnancy test for female volunteers, and a complete blood count.

Taking part in this screening process is entirely your choice. You can decide to refuse to participate in this screening process. If you decide to participate in this screening process, you can then choose to stop taking part at any time for any reason. If you refuse to participate, it will not affect your care or treatment outside this screening procedure, payment for your health care, or your health care benefits. If you consent to the screening process, it does not obligate you to participate in the full study, for which you will be consented separately.

Please read all of the following information carefully. Ask Dr. Greenberg, or his representative, to explain any words, terms, or sections that are unclear to you. Ask any questions that you have about this study. Do not sign this consent form unless you understand the information in it and have had your questions answered to your satisfaction.

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If you decide to take part in this screening process, you will be asked to sign this form. You will be given a copy of the signed form. You should keep your copy for your records. It has information, including important names and telephone numbers, to which you may wish to refer in the future.

New things might be learned that you should know about. The investigators will tell you about new information that may affect your willingness to participate in the screening process.

If you are eligible to participate and decide to be in the study, the Principal Investigator or study MD may still choose to stop your participation in this study if they think it is in your best medical interest, if you are unable to comply with the schedule of study visits, study diets, or study procedures, or if you do not adhere to any and all HNRCA volunteer rules and regulations. If you withdraw or are withdrawn from the study, any data collected from you before your withdrawal will still be used for the study.

As a participant, your identity, medical records, and data relating to this screen will be kept confidential, except as required by law. The U.S. Food and Drug Administration, which regulates investigational drug and device studies, and the study sponsor may also look at screening data that identify you if applicable to the study.

If you have question about your rights as a research study subject, call the Tufts Medical Center and Tufts University Health Sciences Institutional Review Board (IRB) at (617) 636-7512. The IRB is a group of doctors, nurses, and non-medical people who review human research studies for safety and protection of people who take part in the studies. Federal law requires the IRB to review and approve any research study involving humans. This must be done before the screening process can begin.

This screening process has been reviewed and approved by the IRB of Tufts Medical Center and Tufts University Health Sciences.

PURPOSE OF STUDY

This screen is being conducted to determine your eligibility for a study which is designed to determine whether commonly used therapeutics effect the body's ability to absorb and eliminate vitamin B1. We are performing this screen to evaluate your health status to ensure we enroll the right population and minimize risks to our participants. Up to 80 volunteers will be screened for participation in this study, with the goal of enrolling seven subjects.

SCREENING PROCEDURES

If you choose to participate in the screening visit, you will sign this informed consent form and then will be asked to complete the following procedures to determine your eligibility to the main study. This screening visit should take approximately two hours. For this visit, you have been

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asked to come in fasted for 12 hours (nothing to eat or drink except water) prior to your visit. The screening visit will proceed as follows:

1. You will be asked to complete the health questionnaire that was mailed to you if you do not bring the completed form to the visit. This will include the review of any prescription or over-the-counter medications and dietary supplements that you currently take in order for us to understand your health history and any potential risks that may be associated with your participation in the study.
2. Your temperature, heart rate, blood pressure, height and weight will be measured.
3. A member of the MRU nursing team will obtain a detailed medical history and review the study inclusion and exclusion criteria to determine your eligibility to participate in the research study.
4. You will be asked to provide a 20mL blood sample (approximately 4 teaspoons) which will be drawn from a vein in your arm. This will be for standard laboratory testing including Complete Blood Count with differential (CBC) and a comprehensive chemistry profile, metabolic panel, and a pregnancy test on pre-menopausal women only. Women of childbearing potential must agree to use a reliable method of birth control (hormone/barrier) to avoid becoming pregnant during participation in the study. Men will also be asked to use birth control (barrier) and avoid fathering a child while participating in this study.
5. A urine sample will be collected from all participants.
6. Once these tests have been completed, you will have a standard breakfast (muffin or bagel, coffee or tea, and orange juice) at the HNRCA.
7. You will meet with the study dietitian (Dr. Helen Rasmussen) to review your diet habits, diet history, food allergies, diet intolerances, and supplements you take.

Your screening blood test results will be mailed to you within approximately 1-2 weeks. If the results of these tests are outside the accepted ranges for this study, you cannot be in this study.

If the results of these tests are inside of accepted ranges for this study and you decide to participate in the main study, you will be asked to return for nine more study visits.

POTENTIAL RISKS OF SCREENING PROCEDURES

Risk to you should be minimal. Potential discomforts may include irritation and/or pain at the site of the blood draw. You may ask to withdraw your consent and stop participation at any point in time. To protect you from loss of privacy, only the research staff will have access to the samples and records obtained. Information from this screen used for scientific publication will not contain any identifying information.

BENEFITS

There are no direct benefits to you from participation in this study. While these types of studies are unlikely to offer direct benefit to you at the time of your involvement, the information gained may be used to develop new therapies and/or revise dosing guidelines to improve survival or quality of life for you or other people like you in the future.

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ALTERNATIVES

An alternative is to not participate in this study. You can receive the drugs and supplement being used in this study over-the-counter (thiamine) or with a prescription (metformin and trimethoprim) at your local pharmacy.

RESEARCH RELATED INJURY

Emergency medical treatment will be given to you if you are hurt or get sick as a direct result of being in this screening process. You or your insurance carrier will be required to pay for any such medical care. Any needed medical care is available at the usual cost. All needed facilities, emergency treatment, and professional services are available to you, just as they are to the general public. The institution will not pay for your treatment if you become ill or injured as part of this screening process.

COSTS

There are no costs to you or your insurance carrier associated with participation.

PAYMENT

For participation in and completion of the screening process you will receive $25 to compensate for your travel and parking cost. The payment will be mailed in the form of a check approximately 2-3 weeks after the visit.

However, in the event of a government shutdown or other emergency situation, payments will be delayed until the shutdown/emergency ends and all systems are restored at the HNRCA.

Due to federal tax law, you are required to provide us your social security number in order to process your payments. If you receive over $600 from Tufts University Health Sciences in a single calendar year (either from a single study or multiple studies), you will be issued an IRS 1099 form. This may affect your taxes. Only payments for being in research studies will be used to decide if you should receive the IRS form. Money for study-related parking, food, and other expenses are not included in this IRS disclosure.

If you are an employee in this institution and qualify to participate in the study, you cannot participate as a volunteer during hours in which you are being compensated by Tufts University for your regular work. You cannot use vacation, personal days and sick time to participate in the study.

PRIVACY AND CONFIDENTIALITY

The records identifying your name will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. The results from the screen will only be published or presented as group data. No individual participants will be

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identified. Data forms will be identified with a unique study number and kept locked in the study office.

The blood and urine samples you provide will be labelled with unique identifiers and transferred to the Nutritional Evaluation Laboratory at the HNRCA, as well as laboratories at University of California, San Francisco, University of California Davis, and other collaborators deemed fit by the principal investigator. Samples will be coded and de-identified and only the Principal Investigator would be authorized and able to perform re-identification.

Your personal information will not be given to anyone unless we receive your permission in writing. It will only be given if the law requires it. It will also only be given for regular hospital treatment, payment, and hospital management activities.

We will make every effort to keep your information private, but it cannot be completely guaranteed. Certain government agencies (Office for Human Research Protections, Department of Health and Human Services, Food and Drug Administration, National Institute of Health) and the Institutional Review Board of Tufts Medical Center and Tufts University Health Sciences, may check records that identify you. This might include your medical or research records and the informed consent form you signed. The records of this screen might also be reviewed to make sure all rules and guidelines were followed.

A description of this clinical trial will be available on http://www.Clinical Trials.gov, as required by US Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this web site at any time.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care

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provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

If you sign this document, you give permission to the Principal Investigator named above and research staff at Tufts University Health Sciences as well as other individuals at Tufts University Health Sciences who may need to access your information to do their jobs (such as for treatment, payment (billing) or health care operations) to use or disclose (release) your health information that identifies you for the screening process described above.

The parties listed in the preceding paragraph may disclose the health information described below to the following persons and organizations for their use in connection with the research study:

- Individuals or organizations working under the direction of the Principal Investigator(s) for the study,
- Outside individuals or entities that have a need to access this information to perform activities relating to the conduct of this research, such as analysis by outside laboratories on behalf of Tufts University Health Sciences
- Other researchers and institutions that are conducting or participating in this study,
- The study sponsor, The National Institutes of Health, and any companies that they use to oversee, manage, or conduct the research,
- The Office for Human Research Protections in the U.S. Department of Health and Human Services, the United States Food and Drug Administration (FDA) and other federal and state agencies that have the right to use the information as required by law, and
- The members and staff of any Institutional Review Board (IRB) and Data and Safety Monitoring Board that oversee this study.

The health information that we may use or disclose (release) for this screening process includes all information in your medical record including the record of your care, as well as any information collected or created during the course of this study.

Tufts University Health Sciences is required by law to protect your health information. By signing this document, you authorize Tufts University Health Sciences to use and/or disclose (release) your health information for this screen. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You may not be allowed to see or copy the information described on this form as long as the research is in progress, but you have a right to see and copy the information upon completion of the research in accordance with hospital policies.

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You can decide to sign or not to sign this form. However, if you choose not to sign this form, you will not be able to take part in the screening process.

This authorization does not have an expiration date. You may change your mind and revoke (take back) this authorization at any time. Even if you revoke this authorization, this site's clinical, administrative and research staff may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this authorization, you must write to: HIPAA Privacy Officer for Research, 800 Washington Street, Box 5100, Boston, MA 02111. If you revoke this authorization, you may no longer be allowed to participate in the screening process described in this form.

WHOM TO CONTACT

Should you have any problems or questions about this research study and our screening procedures, you may contact Dr. Andrew Greenberg, the study Principal Investigator, at:

Dr. Andrew Greenberg
HNRCA
711 Washington Street
Boston, MA 02111

You could also call Dr. Greenberg at his office (617) 556-3144 during daytime (9am to 5pm) or email him at andrew.greenberg@tufts.edu

For emergencies at any time, including days, evenings, weekends and holidays, please call (617) 230-7545 to reach Dr. Ceglia, the study physician.

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Documentation of Consent

I have been given a copy of this form. I have read it or it has been read to me. I understand the information and have had my questions answered to my satisfaction. I agree to take part in this study.

I understand that I will be informed of any new findings developed during the course of this research study that may affect my willingness to stay in this research study.

_____ _____
Date Participant's Signature

I have fully explained to _____ the nature and purpose of the above-described study and the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____ _____
Date Principal Investigator or Representative's Signature