PRINCIPAL INVESTIGATOR: [redacted]

STUDY TITLE: Evaluation of Oral Minocycline in the Treatment of Geographic Atrophy Associated with Age-Related Macular Degeneration

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: January 12, 2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

[redacted]

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Age-related macular degeneration (AMD) is the leading cause of vision loss in Americans 60 years of age and older. It affects the macula, the central part of the retina needed for sharp, clear vision and activities such as reading, sewing and driving.

There are two types of AMD, wet and dry. In dry AMD, cells in the macula die. The advanced form of dry AMD is called geographic atrophy or GA, which results when light-sensitive cells in the macula die to an extent that causes central vision to decrease.

The purpose of this study is to evaluate whether a drug called minocycline is safe to give to people with GA and if it can help preserve vision in people with GA. GA may be partly caused by inflammation. Minocycline is a drug that might prevent inflammation and therefore might reduce GA.

Minocycline is approved by the FDA as an antibiotic. Minocycline has not been studied before as a treatment for GA.

HOW MANY PEOPLE WILL TAKE PART IN THIS RESEARCH STUDY?

Up to 60 people with GA associated with AMD will be enrolled at the NEI as well as one other clinic.

HOW LONG WILL YOU TAKE PART IN THIS RESEARCH STUDY?

You will be followed under this research study for at least three years and nine months. The study requires a minimum of 11 visits to the NEI outpatient clinic. These visits will occur every three months for the first 15 months then every six months for the next two and a half years. Each visit will take about eight hours (a full work day). If we are unable to finish all the required testing in one day, we may ask you to return to the clinic within 10 days to complete all the testing. The study is intended to end when all participants have been followed for three years and nine months. Hence, if you are enrolled at the beginning of the study, you may be followed up to five years, although your participation may still end earlier.

You will stay under the care of your own doctors for your general medical care while you are in this study. You should tell all of your own doctors about this study and that you will be taking minocycline, so that they can avoid drug interactions that might be dangerous.

WHAT DO WE DO TO DECIDE IF YOU ARE ELIGIBLE FOR THIS RESEARCH STUDY?

Your NIH doctor will perform a medical examination, including taking your medical history, a brief general examination and a complete eye examination to determine if you are eligible to receive the study medication. Most of these tests are a standard part of a complete eye examination. These tests will take place in the NIH outpatient eye clinic and will take about four hours (half a work day). If only one eye meets the study criteria, it will be designated the "study eye." If both eyes meet study criteria, we will choose one eye as the "study eye," with the other eye designated as the "qualifying fellow eye." We will draw blood by placing a needle in a vein in your arm to test blood count and blood chemistries. If you are a woman who is able to get pregnant, you will have a pregnancy test. If some of these tests have already been done under another NEI study, we may use them to determine your eligibility.

WHAT PROCEDURES, DRUGS, OR OTHER TREATMENTS ARE INVOLVED IN THIS RESEARCH STUDY?

If you are eligible to participate, you will start taking the study medication, minocycline, at your fourth visit. You will start taking the study pills the evening of the fourth study visit. You will take one pill twice a day for at least three years. You should take one pill in the morning and one pill in the evening, at about the same time each day, about 12 hours apart.

After the sixth visit you will return for an outpatient study visit every six months. You will need to bring your pill bottle with any unused study pills to each visit.

At each visit, we will ask you about your health and what medications you are taking. Please tell us about any changes in your medications that your own doctors may have made.

At each study visit, you will have some or all of the following tests:

Eye Examination and Photography: The eye examination includes testing how well you see, measuring your eye pressure and checking your eye movements. To examine the inside of your eyes, we will use eye drops to dilate your pupils. While your eyes are dilated, we will measure the thickness of your retina and take pictures of the retina and the inside of your eye.

Thyroid Gland Examination: We will examine the thyroid gland in your neck. We will feel your thyroid gland while you swallow. If the examination suggests a possible problem with your thyroid gland, you will be referred to an endocrinologist.

Microperimetry: We will test how well you can detect different levels of light. You will be seated in front of a computer screen and asked to press a button when you see a light on the screen.

Fluorescein Angiography: For fluorescein angiography, an intravenous line will be placed in a vein in your arm. The intravenous line will be used to give a dye called "fluorescein." The dye will travel through your veins up to the blood vessels in your eyes. A camera will be used to take pictures of the dye as it flows through the blood vessels in your eyes.

Blood Tests: Blood will be drawn for blood chemistries, blood cell counts and thyroid tests. Blood will be drawn at several study visits. We will draw no more than four teaspoons of blood at one time and no more than a ¾ cup of blood during the entire study.

Pregnancy Testing: Minocycline can be harmful to a developing fetus. Therefore, women who are able to become pregnant will have a pregnancy test before starting on minocycline and while taking it. You will not be able to start or continue taking minocycline if the pregnancy test is positive. If you are able to become pregnant and are sexually active, you must be willing to use two effective methods of birth control. A gynecologist will advise you on the acceptable methods of birth control.

In between consecutive study visits, we may contact you by telephone to inquire about any health issues you have, any changes in your medications, and issues related to taking the study drug.

WHAT ARE THE RISKS AND DISCOMFORTS OF THIS RESEARCH STUDY?

Risks of Minocycline: Minocycline is an antibiotic. It is widely used to treat infections. The most common side effects of minocycline are diarrhea, upset stomach or abdominal pain.

Minocycline can make your skin and eyes sensitive to sunlight and can cause dark patches on the skin. Exposure to sunlight, even for brief periods of time, may cause a skin rash, itching, redness or other discoloration of the skin, or severe sunburn. When you take this medicine, you should:

- Wear protective clothing, including a hat and sunglasses whenever you are outside.

- Apply a sun block product that has a skin protection factor (SPF) of at least 15 to your skin and a sun block lipstick to your lips. Some participants may require a product with a higher SPF number, especially if they have a fair complexion.
- Use extra caution near water, snow, and sand because they reflect and intensify the damaging rays of the sun.
- Not use a sunlamp or tanning bed or booth.

You may still be more sensitive to sunlight or sunlamps for two weeks to several months or more after stopping minocycline. If you have a severe reaction, see your doctor immediately.

Light-headedness, dizziness and vertigo have been reported with minocycline.

A potentially fatal reaction called "Drug Rashes with Eosinophilia and Systematic Symptoms (DRESS)" has been reported with minocycline use. You should contact the study team or your own doctors immediately if you develop a new rash.

Some cases of thyroid cancer have been reported in people taking minocycline. We will monitor you for signs of thyroid cancer by examining your thyroid and by blood tests. If needed, we will refer you to an endocrinologist for further evaluation.

If you are receiving an anticoagulation treatment using a drug called warfarin (Coumadin), minocycline can affect how well the medication works, requiring the dose of the medication be adjusted to achieve its desired effect 2-4 weeks after starting minocycline. If this is not done, the anticoagulation treatment may not be effective and may reduce the beneficial effects of warfarin or add to its side effects.

If you are currently taking warfarin you will be asked to visit your prescribing physician within 2-4 weeks to have your anticoagulation regimen assessed.

Other rare but potentially severe side effects of minocycline include allergic reactions (rash, hives, itching, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips or tongue), bleeding or discharge from the gums, bloody stools, blurred vision, decreased hearing, fever, headache, inflammation of the pancreas (which can cause stomach tenderness, nausea, vomiting, increased pulse rate), abnormal thyroid function, joint pain, muscle pain or weakness, or liver toxicities. We will treat these if they occur.

If you develop side effects, including, but not limited to those listed above, or have to stop taking minocycline for any reason, we ask that you notify us immediately.

Even if you stop the study pills, we ask that you continue to come for the remaining study visits so that we can follow your GA.

Please be aware that minocycline can change the effectiveness of particular medications (e.g. penicillin).

CAUTION: MINOCYCLINE CAN HARM A FETUS. Both men and women need to use contraception while in this study.

Minocycline can lower sperm count. We do not know if a child fathered by a man taking minocycline could be affected.

Minocycline can harm a fetus when taken by a pregnant woman. It can cause permanent yellow-grey-brown discoloration of the child's teeth. Minocycline passes into breast milk and can cause permanent discoloration of the teeth of a nursing infant. Therefore, women who are pregnant, nursing, or wishing to become pregnant, cannot participate in this study. Men should avoid fathering a child while in this study.

Women who are able to get pregnant will have a pregnancy test done at each study visit. If you or your partner becomes pregnant while participating in this study or suspect that you might be pregnant, you must tell us immediately. The doctor will advise you of the possible risks to your unborn child and options available to you. If you become pregnant, we will stop the minocycline immediately and you will be withdrawn from the study.

Risks of Eye Examination, Dilation and Photography: There is minimal medical risk from the tests of vision, measuring eye pressure and eye photography. During the exam, the eye drops used to dilate your eyes may sting. You may have glare and blurry vision for several hours while your eyes are dilated. Some people are allergic to eye drops, while others experience a temporary increase in eye pressure. Your eye could become red or painful. These problems will be treated if they occur.

Risks of History, Physical Examination and Microperimetry: Please note that this physical examination is for research purposes only and does not replace any examination you may receive from your own physicians. There is minimal medical risk and minimal discomfort from these tests.

Risks of Fluorescein Angiography: The dye may cause your skin to turn yellow for several hours. Because the dye passes through your kidneys, your urine will turn dark orange for up to 24 hours after the exam. Some people feel nauseous for a few seconds during the fluorescein angiogram. The fluorescein dye can leak out of your vein during the injection and cause the skin to feel mildly uncomfortable or become

yellow. The mild discomfort usually lasts only a few minutes, and the yellow color goes away in a few days. In rare cases, there is an allergic reaction to the dye, which causes a rash and itching. Allergic reactions are treated by antihistamines, given by pills or a shot if needed. Severe allergic reactions that cause difficulty breathing and a drop in blood pressure can be life-threatening but are very rare. This would be treated immediately. Please let your doctors know if you have ever had an allergic reaction to fluorescein.

Risks of Drawing Blood: You may have some discomfort and bruising at the site of needle entry. There is a very small risk of fainting. Infection in the area of the needle insertion is rare.

ARE THERE ANY BENEFITS TO YOU IF YOU TAKE PART IN THIS RESEARCH STUDY?

You may benefit from participating in this study if you receive minocycline and it helps to decrease the rate of vision loss. We are however uncertain about how much, if at all, minocycline may decrease the rate of vision loss. In any case, your participation will contribute to knowledge that may help treat others with this disease in the future.

WHAT OTHER CHOICES DO YOU HAVE?

A combination of vitamins and supplements including high doses of vitamins C and E, beta carotene and zinc (known as the AREDS formulation) has been shown to decrease the progression to wet AMD which is the more rapidly progressive form of AMD. You will be able to take these supplements during the course of this study. There are no treatments which have been shown to decrease the worsening of GA.

Minocycline is an FDA-approved antibiotic. You may not have to participate in this study to receive minocycline. Your own doctor may be able to prescribe minocycline for you as an "off-label" use.

ARE THERE REASONS THAT YOUR RESEARCH PARTICIPATION MAY END EARLY?

You can withdraw from this study at any time without losing any of the benefits to which you may otherwise be entitled. We may remove you from the study if medical problems develop or if you are unable to comply with the requirements of the study. We will remove you from the study if you need to start a medication that cannot be taken safely with minocycline. We will remove you from the study if you require a treatment that is not permitted in this study.

This study is under review by a Data and Safety Monitoring Committee (DSMC). A DSMC is an independent group of doctors, scientists and ethicists. The DSMC can stop or change the study early if they determine that the study medications are not working, or that the study's goals have been met or cannot be met. If the study is stopped, your participation will end.

WHAT WILL HAPPEN WHEN THE RESEARCH STUDY IS OVER?

When the research study is over, you will stop taking the study pills. You will continue to receive care from your regular eye doctor during and after this study. You may be offered participation in another NIH study, if one is available.

WILL YOUR CLINICAL AND OTHER TEST RESULTS BE SHARED WITH YOU?

We will give you the results of all of your examinations. With your written request, we will send reports to your own doctors.

WILL THE RESULTS OF THIS RESEARCH STUDY BE SHARED WITH YOU?

We will share with you any information we learn that may affect your willingness to continue to participate in the study in a timely manner.

WILL ANY OF YOUR BLOOD, TISSUE, OR OTHER SAMPLES BE STORED AND USED FOR RESEARCH IN THE FUTURE?

None of your blood will be stored or used for future research.

DO ANY OF THE RESEARCHERS OR THE NIH HAVE A FINANCIAL INTEREST RELATED TO THIS RESEARCH STUDY?

None of the doctors in this study receives money or has a conflict-of-interest for doing this study.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

We can assist you if you have problems related to transportation to the NIH. Accommodations may be provided when an overnight stay is necessary.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. 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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Eye Institute and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.

- National Institutes of Health Intramural Institutional Review Board

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made

by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, [redacted] Other researchers you may call are: [redacted] You may also call the NIH Clinical Center Patient Representative at [redacted] or the NIH Office of IRB Operations at [redacted], if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.