Adalimumab vs. Conventional Immunosuppression for Corticosteroid-sparing for Uveitis (ADVISE) Trial

Adult Consent

Version date November 8, 2021

ClinicalTrials.gov identifier: NCT03828019

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

INFORMED CONSENT DOCUMENT

Adult consent

Study Title: Adalimumab vs. Conventional Immunosuppression for Corticosteroid-sparing for Uveitis (ADVISE) Trial

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IRB No.: 00009196

Funded By: National Eye Institute of the National Institutes of Health

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Key information about this study

- We are asking you to volunteer for a research study of treatments for non-infectious uveitis. You do not have to join the study; it is your choice and there is no penalty for not joining. Ask as many questions as you need to help you make your decision. Please review the details about the study described in the rest of this consent document before deciding about joining the study.
- In the study you will receive standard treatments for uveitis. You and your doctor will not have a choice to which drugs you receive. You will receive the same kind of care and monitoring that you would get outside the study. We do not know if being in the study will benefit you more than if you received similar care outside of the study.
- The study is being conducted to see whether adalimumab (Humira) or conventional immunosuppressive drugs works better to control uveitis and allow the dose of prednisone to be reduced to 7.5 mg/day or less. You are being asked to participate because you have intermediate, posterior, or panuveitis that requires a dose of prednisone that is greater than 7.5 mg/day.
- If you join, you will be randomly assigned by computer to receive either adalimumab or a conventional immunosuppression drug in addition to prednisone.

- If you are assigned to adalimumab, the study will provide the adalimumab. Adalimumab is given by injection under the skin on the thigh or abdomen. If you are assigned to receive adalimumab, we will teach you (or a care-giver) how to give an injection at the first study visit. We will give you the first injection. After that you will give yourself an injection on the same day (in the clinic). Then you will give yourself an injection one week later and then every other week at home for the rest of the study. The most common side effects of adalimumab are redness, itching, pain or swelling at the injection site, which is reported in 20% of patients. If you are assigned to receive adalimumab, it will be provided free of charge because it has been donated by the drug company AbbVie.

  If a second study drug (a conventional immunosuppressive drug) needs to be added to adalimumab to treat your uveitis, it will be charged to your insurance and you will be responsible for any co-payments. The study will reimburse you for co-payments up to $1500 for conventional immunosuppressive drugs you were prescribed as part of the study.

- If you are assigned to conventional immunosuppression, your doctor will prescribe one of five different conventional immunosuppressive drugs. Conventional immunosuppressive drugs are usually given by mouth in the form of a pill. The side effects depend upon the type and dose of the particular drug. Your doctor will explain the side effects of these drugs, each has different side effects. You and your doctor will select the best one for you. You should fill the prescription and start taking the drug as soon as possible. The cost of the drug will be charged to your insurance and you will be responsible for any co-payments. The study will reimburse you up to $3000 for co-payments for immunosuppressive drugs prescribed for you as part of the study.

- All participants will also take prednisone. Your doctor may change the type and dose of the study drugs prescribed to treat your uveitis depending upon how well the study medications work for you.

- The study will include 10 study visits at the clinic and last for one year. At the study visits we will do eye examinations, take pictures (digital images) of the insides of your eyes, perform vision tests, draw blood, and ask you to answer questions about your health

and well-being. The first study visit will take 4 to 5 hours, later visits should be shorter (about 2 to 4 hours). You will receive $75 for each study visit. If you complete all 10 visits you will receive a total of $750.

- The study will only pay for tests and procedures that would not be done as part of your usual care for uveitis. You or your insurance company will be charged for your regular medical care for uveitis.
- The information above is a brief summary of the study. If you are interested in joining the study, it is important to read the entire consent statement.

Purpose of research project

This study is evaluating treatments for uveitis, which is an inflammation inside of the eye. The types of uveitis being studied can cause vision loss. Treatment helps to avoid vision loss. This study compares two kinds of drugs for treatment of non-infectious uveitis that requires more than an oral corticosteroid to control. The two kinds of drugs are adalimumab and conventional immunosuppressive drugs. Both treatment regimens are commonly used to treat uveitis.

The first-line treatment for uveitis is an oral corticosteroid drug like prednisone. Often a high dose of prednisone is needed to control the inflammation. Because high doses of prednisone can lead to side effects like weight gain and increased blood pressure, patients who need high doses of prednisone are often given immunosuppressive drugs to help control inflammation. Adding immunosuppressive drugs allows the dose of prednisone to be reduced over time.

The immunosuppressive drugs that have been typically used to treat uveitis include drugs like methotrexate, mycophenolate, azathioprine, cyclosporine, and tacrolimus. We refer to these drugs as “conventional immunosuppressive drugs.” Conventional immunosuppression drugs are not approved by the FDA for treatment of uveitis, however they are approved for other conditions involving inflammation and are commonly used to treat uveitis. Adalimumab will be compared to the conventional immunosuppressive drugs in this study. Adalimumab is a newer kind of immunosuppressive drug called a biologic. It was approved by the FDA specifically for the treatment of uveitis in 2016. It is also used to treat other inflammatory conditions.

Both conventional immunosuppression and adalimumab are used in clinical care to allow the dose of prednisone to be reduced or stopped without an increase in uveitis inflammation. We are doing this study to find out which is better at keeping uveitis under control on lower doses of prednisone, conventional immunosuppressive drugs or adalimumab.

This study is funded by the National Eye Institute (NEI), a part of the National Institutes of Health (NIH). The NIH is a United States government agency.

The drug company AbbVie is donating adalimumab for this study. AbbVie has no role in the design, decision making, conduct, or interpretation of the study results.

Why we are asking you to participate

You have non-infectious uveitis that needs treatment with an oral corticosteroid drug such as prednisone. Because of the severity of your uveitis, treatment with immunosuppressive drugs also is recommended according to standard treatment guidelines. In this study you will receive either adalimumab or conventional immunosuppressive drugs in addition to oral corticosteroids to treat your uveitis.

About 222 patients will participate in this study at clinics in the United States, Australia, Canada, and the United Kingdom. Up to 40 participants will participate at this clinic.

Study procedures

Screening and baseline phase

If you agree to take part in this study and sign this consent form, we will need to find out if you are eligible and collect baseline information. The procedures for checking eligibility and collecting information about you are listed below. Most are done as part of the usual clinical care for uveitis.

- We will ask you about your medical history, eye problems, and treatments you have had for uveitis.
- Your eyes will be examined by the study doctor. Drops will be placed in your eyes before the exam to make the pupils larger. This will make it easier for the doctor to see inside of your eyes. The doctor will use a tool called an ophthalmoscope to see the inside of your eyes.
- Your vision will be tested by asking you to read letters on a chart.

- Your height, weight, and blood pressure will be measured.
- You will have digital images of the back of your eyes taken.
- You will have an optical coherence tomography (OCT) scan to get images of your retinas at the back of your eyes. The scan is like an ultrasound of your eye, except it uses light instead of sound waves.
- You will have about 18 mL (a little more than a tablespoon) of blood taken from your arm. The blood will be used to test for tuberculosis (TB), hepatitis B and C, and for standard blood tests required for treatment. These tests will be done by the laboratory the clinic typically uses for blood testing.
- You will fill out questionnaires about your health and vision and how they affect your life. This is done for the study, not as part of usual care for uveitis.
- If you are able to become pregnant, you will have a pregnancy test. The test will be done on a urine sample. You may not be in the study if you are pregnant or nursing.

You also may be asked to sign a medical release form that will allow the study doctor to get information from your medical records from other doctors.

If you have a certain type of intermediate uveitis, you will need to have another test to make sure you don't have multiple sclerosis (MS) or another demyelinating disease and that it is safe for you to enroll in the study. The next three paragraphs describe the test.

- You will have a magnetic resonance imaging (MRI) scan of your brain. The MRI will be done to look for evidence of a demyelinating disease, such as MS, in your brain. Certain types of intermediate uveitis are sometimes associated with MS. If the MRI shows brain changes that might be from a demyelinating disease, you cannot be in the study. This is because one of the drugs used in this study might make such diseases worse.
- A drug containing a metal called gadolinium will be injected into your arm before the MRI. It makes it easier for the doctor see if there is evidence of MS in your brain than an MRI taken without use of the drug. MRI scans create images using a magnet and radio waves. There is no radiation involved in this test.

- The MRI machine is like a large tube. You will lie flat on a platform and then the platform will slide inside of the tube. You will need to stay still. The machine will make loud banging noises. The scan will take about 20 minutes. Your total time at the imaging facility will be about one hour.

If you have certain types of uveitis, you will need to have other tests, such as a visual field test or additional images of your eyes. The results of the test will be used to monitor your uveitis. You will only undergo the tests below that are relevant to the type of uveitis you have.

- A visual field test that checks your side vision (peripheral visual field) is used to evaluate uveitis characterized by small spots on the back of the eye (birdshot uveitis).
- A special kind of photograph of your eyes called fundus autofluorescence is used to evaluate uveitis that is characterized by inflammation throughout the eye (choroiditis).
- A photography test called fluorescein angiography is used to evaluate uveitis that involves inflammation of the branches of the retinal artery (retinal vasculitis). For this test a dye is injected into a vein in your arm or hand. The dye will move through your bloodstream, including the blood vessels in the back of your eyes. A series of images will be taken. The doctor evaluates the images to see where blood vessels are inflamed and severity of the inflammation. The test takes about 20 minutes.

Study treatment

If you are eligible and you complete the baseline procedures described above, you will be enrolled in the study. Everyone in the study will be treated with oral corticosteroids. The most common type of oral corticosteroid used is prednisone. It will be given according to the established standards for treating uveitis. In addition to treatment with oral corticosteroids, you will be randomly assigned by a computer program to receive either adalimumab or conventional immunosuppression. You will have an equal chance of receiving adalimumab or conventional immunosuppression as your study treatment. Your study doctor will not get to choose which of these two study treatments you receive.

If you are assigned to receive adalimumab, it will be given by subcutaneous injection (injection right under the skin). The first dose will be given in the

clinic as described below. After that you or a care-giver (for example a relative or friend) will give the injections at home. We will teach you (or the care-giver) how to give the injection.

- The first dose will be given at the clinic so that we can monitor you for any adverse reactions to the drug and teach you (or the person you choose) how to give the injection. The first dose will be higher than the dose you will receive for the rest of your time in the study. This higher dose, 80 mg, is called a loading dose. It is given to help the treatment work faster. The first dose will be given in two injections at the clinic. We will administer the first injection and show you (or the person you choose) how to do it. Then you (or the person you choose) will give the second injection to yourself (you) in the clinic under observation.
- From then on you will give yourself the injection (or the person you have chosen and has been trained will give you your injection) at home according to the following schedule. One week after your first dose in the clinic, you will give yourself one injection (40 mg) at home. After that you will give yourself an injection of 40 mg every other week for the rest of the study. We will provide you with adalimumab to take home with you.

If you are assigned to receive conventional immunosuppression, your study doctor will decide which conventional immunosuppressive drug, or combination of drugs, you will receive. The doctor will use guidelines established by uveitis experts to select the drug. The type of uveitis you have and other health conditions will be considered. Most of these drugs are taken by mouth.

- The conventional immunosuppressive drugs that may be used are: methotrexate, mycophenolate, azathioprine, cyclosporine, and tacrolimus.
- Sometimes two of these drugs are used together so you may be asked to take 2 immunosuppressive drugs at the same time. Depending on your situation, you may receive one or two of these drugs as your study treatment.
    - If you are already taking one of these drugs when you join the study, you will continue on that drug during the study and one of the other drugs will be added.

- If you are not taking any of these drugs when you join the study, you will be started on one of them.

- Some of these drugs are taken every day. Some are only taken once a week.
- You will be provided with a prescription for the assigned drug. You will be responsible for any co-pay required. However, as described earlier, we will reimburse you for up to $3000 for out of pocket costs for the study-assigned treatments.

No matter which treatment you are assigned to start with, a second drug may be added later if your uveitis is not controlled by the first study drug. The second drug will be a conventional immunosuppressive drug. All of these drugs typically are used in the clinical care of patients with your type of uveitis. If you were assigned to adalimumab and require a second drug to control your uveitis, the study will reimburse you for up to $1500 for out of pocket costs for the second drug.

Study visit schedule

You will be in the study for one year and will have 10 study visits at this clinic. The procedures for the first study visit may be spread out over more than one day. For example, if you need to have an MRI before you enroll, the MRI may need to be scheduled on a different day.

For the first 6 months you will come to the clinic for a study visit every month. After your six-month study visit, you will have a study visit every two months. You may need to come into the clinic more often for clinical care and those visits will not be part of the study. The table on the next page shows what will be done at each study visit. At each follow-up visit, you will have about 10 mL (less than a tablespoon) of blood taken from your arm. The blood will be used for standard tests to monitor for possible side effects of the drugs you are taking.

Most of the procedures done as part of the study visits are usually done as part of standard of care for uveitis. However, standard of care for uveitis may vary by doctor, patient needs, and monitoring requirements for specific treatments. The procedures that are being done that are just for research are the quality of life questionnaires, the type of vision test, and in some cases pregnancy testing and an MRI.

Procedures done at visit are marked with X under visit month										
Visit month	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**10**	**12**
Visit code	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V09**	**V10**
Medical, eye, and treatment history	X	X	X	X	X	X	X	X	X	X
Vision test	X	X	X	X	X	X	X	X	X	X
Measure weight and blood pressure	X	X	X	X	X	X	X	X	X	X
Height	X									
Eye exam	X	X	X	X	X	X	X	X	X	X
Photographs (digital images) of eyes	X						X			X
OCT	X			X			X			X
Quality of life questionnaires	X			X			X			X
Blood draw for complete blood count and chemistry panel	X	X	X	X	X	X	X	X	X	X
Blood test for tuberculosis and hepatitis	X									
Pregnancy test for menstruating individuals	X									
Additional procedures for patients with specific types of uveitis only										
Visit month	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**10**	**12**
Visit code	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V09**	**V10**
MRI of brain *for patients with* ***anterior/intermediate or intermediate uveitis without systemic disease***	X									
Peripheral field test *for patients with* ***birdshot chorioretinitis***	X	X	X	X	X	X	X	X	X	X
OCT will be done at all visits for patients with early stage ***VKH****	X	X	X	X	X	X	X	X	X	X
Fundus autofluorescence photographs *for patients with* ***choroiditis or late stage VKH****	X	X	X	X	X	X	X	X	X	X
Fluorescein angiography *for patients with* ***retinal vasculitis***	X	X	X	X	X	X	X	X	X	X

*Vogt-Koyanagi-Harada disease

Risks/discomforts

If you enroll in the study your treatment will be decided based on randomization. The treatment you are assigned might be different than what you would have received if you did not enroll and instead you and your doctor decided which treatment you would receive. Since the risks of treatment, which are described below, are different for each treatment, you may be exposed to different risks if you enroll than you would be exposed to if you received treatment outside of the study. Based on the results of previous studies, we think the overall risk rate will be about the same for both treatment groups in this study.

Risks associated with each of kind of drug used as study treatment are listed below. Usually the risks can be avoided or reversed if the drug dose is lowered or you stop taking the drug.

Risks associated with oral corticosteroids

All study participants will take oral corticosteroids (for example, prednisone). The most common side effects of oral corticosteroids are:

- Ocular side effects
    - About 6% of patients per year need cataract surgery
    - About 3% of patients per year have increased eye pressure
    - About 1.3% patients per year develop glaucoma
- Water retention, weight gain, headache, muscle weakness, and loss of muscle mass
- Face puffiness, growth of facial hair, easy bruising, acne, and rounding of the upper back
- Irregular menstrual periods
- Mental changes such as trouble sleeping, mood swings, increased energy, and personality changes
- Increased blood pressure, cholesterol, and blood sugar
- Lowered resistance to infections and making infections harder to treat, slow wound healing
- Increased risk of osteoporosis (bone thinning)
- Increased risk of congestive heart failure for those already at risk of it
- Aseptic necrosis of bone is a rare and serious side effect

Serious side effects are rare especially when treatment is managed using the guidelines that will be followed in this study. Side effects occur more often with longer periods of treatment and with higher doses. Side effects usually go away when the dose is lowered or treatment is stopped. An objective of this study is to reduce your dose of oral corticosteroids to the lowest possible dose or even stop it as long as your uveitis is controlled.

In addition to oral corticosteroids, your study treatment will include either adalimumab or a conventional immunosuppressive drug. The risks associated with these drugs are described below.

Risks associated with adalimumab

You may be assigned to receive adalimumab. The risks of adalimumab are listed below.

- The most common side effects are redness, itching, pain, or swelling at the injection site, reported in 20% of patients.
- Less common side effects include an increased risk of infections, particularly tuberculosis, fungal infections, and herpes zoster (shingles).
    - About 7% of patients get an infection that requires treatment with antibiotics in a year.
    - There also may be a small increased risk (less than 1%) of opportunistic infections.
    - Rarely, some of these infections, including an infection of the brain called progressive multifocal leukoencephalopathy (PML), can be life-threatening.

  You should not receive any live vaccines while using adalimumab.
- Uncommon side effects include
    - Nausea, vomiting, abdominal pain, or diarrhea
    - Reversible bone marrow suppression
    - Reversible liver damage
- Rare side effects include
    - Development of anti-adalimumab antibodies and a lupus-like syndrome
    - Worsening of demyelinating disease, such as multiple sclerosis

- Cancers, including lymphoma, have been reported in some patients using these types of drug. Cancers occur commonly in the general population. Published reports analyzing information from eye patients suggest the risk may not be increased by use of this kind of drug. However, some studies suggest that use of these drugs may increase the risk of non-melanoma skin cancer.

Risks associated with conventional immunosuppressive drugs

If you are assigned to conventional immunosuppression, your study treatment will be one or two conventional immunosuppressive drugs. Your initial study treatment will be one drug; a second could be added later in the study if it is needed to control your uveitis. If you are assigned to adalimumab as your study treatment, a conventional immunosuppressive drug may be added later in the study if needed to control your uveitis.

Different drugs are used for conventional immunosuppression, you and your doctor will decide which of these is the best drug (or drugs) for you. These drugs will be given according to established standards. Some of these drugs require routine testing of blood to be given safely. Your doctor will talk to you about the specific side effects of the drugs you receive. The risks associated with conventional immunosuppressive drugs are described below.

- In general, side effects can affect the kidney, liver, GI tract, and bone marrow.
- These drugs may lower your resistance to infections.
    - About 7% of patients get an infection that requires treatment with antibiotics in a year.
    - There also may be a small increased risk (less than 1%) of opportunistic infections.
    - Rarely, some of these infections, including an infection of the brain called progressive multifocal leukoencephalopathy (PML), can be life-threatening.
- Most side effects are reversible if the dose of the drug is lowered or if the drug is stopped. In general, these drugs have to be stopped due to side effects 10-20% of the time. If a drug needs to be stopped due to side effects, your doctor may start another immunosuppressive drug as a replacement treatment. Your doctor will discuss with you the best treatment for you.

- Cancers, including lymphoma, have been reported in some patients using these types of drug. Cancers occur commonly in the general population. Published reports analyzing information from eye patients suggest the risk may not be increased by use of this kind of drug. However, some studies suggest that use of these drugs may increase the risk of non-melanoma skin cancer.

- Pregnancy risks for both genders – Some of these drugs are associated with an increased risk of first trimester pregnancy loss and birth defects. These risks apply to men as well as women because the drugs may affect sperm cells. Problems can result if you are using one of the drugs before you become or while you are pregnant or if you are using one of the drugs before or at the time you impregnate someone. You may not join this study if you plan to become a biological parent (get pregnant or impregnate someone) in the next 18 months. If you are a person who can become pregnant, you will have a pregnancy test at your first study visit.

  If you are pregnant or breastfeeding, you cannot join this study.

  If you are able to become pregnant or impregnate someone, you must agree to practice birth control while you are in the study and for 6 months after you complete the study. The acceptable forms of birth control are abstinence, combination barrier and spermicide, hormonal or intrauterine device. Your doctor will talk to you about risks if you are taking specific drugs that are known to cause problems in pregnancy. If you or your partner become pregnant during the study, you must agree to let the study doctor know immediately. You must agree to report any problems during the pregnancy and the outcome of the pregnancy.

Your doctor will talk to you about the specific side effects for the drugs you are taking.

Other risks

As with all research studies, this study may involve unknown risks. Any unknown risks you are exposed to in the study are likely to be the same risks you would have if you were being treated for uveitis outside of the study. You will be told of any findings that might change your decision about continuing in the study.

Your uveitis may not get better or could get worse. Uveitis getting worse or failing to improve is unlikely because oral corticosteroids and immunosuppression is the standard treatment and known to be effective for most cases. If the study treatments do not work, your doctor may change your treatment according to best medical judgment.

If you have any questions or concerns regarding any of these risks, please talk to your study doctor. If you experience any illness or discomfort during the study, you should notify your study doctor.

The risks associated with study procedures are minimal. Most of the study procedures are part of standard care for patients with the type of uveitis you have. The risks include:

- Discomfort, bruising, or swelling at the site of your blood draw.
- Discomfort from bright lights used while taking images of your eyes.

If you have a certain type of intermediate uveitis you will need to have an MRI of your brain before you can join the study. The MRI will be conducted at an imaging center. A drug containing gadolinium will be injected into a vein in your arm before the MRI to improve the MRI's ability to detect disease. The doctor or staff at the imaging center will discuss the risks of the MRI and the drug with you. The main risk of the MRI is feeling uncomfortable and closed in while you are in the MRI machine. Risks associated with the injection of the drug include:

- You may experience headache, nausea, and dizziness for a short time.
- You may get an unpleasant taste in your mouth.
- You may feel hot, numbness, or tingling, have itching or a rash.
- You may have a feeling of cold, warmth, pain, or burning at the injection site.
- Some people can have an allergic reaction to the drug. Sometimes the reaction can be serious.
- For people with kidney problems there is a risk of developing a condition called scleroderma. This is very uncommon. Scleroderma involves thickening of the skin, muscles, and organs. You should let the radiologist know if you have kidney disease.

Some types of uveitis need to be monitored by fluorescein angiography. If you have one of these types of uveitis, you will have this procedure at every study visit.

- You may experience pain or bruising where the dye is injected into your hand or arm.
- You may have nausea or vomiting from the injection, however, this usually lasts only a short time.
- The dye used in this procedure may make your skin look darker for one or two days after the test. Your urine may be orange after the test.
- Some people can have an allergic reaction to the fluorescein dye. Rarely the allergic reaction is severe enough to cause the person to go to the hospital. This happens in less than 1 in 10,000 tests.

Benefits

You will receive standard treatments for uveitis; all of these treatments have been shown in research studies to be effective for the treatment of non-infectious uveitis. There are no experimental treatments in this study. The benefits of taking part in this study for you are unknown because it is not clear which treatment will work best for which patients. Information from this study may be helpful in the future to other people with uveitis. The information also may help you because you may need treatment for uveitis in the future.

Payment

You will receive $75 for each study visit. If you complete all 10 visits you will receive a total of $750. If you leave the study before finishing all visits, you will be paid for the visits you have completed. If you receive $600 or more in one year from this study or combined with payments from other studies you participated in at this institution, these payments will be reported to you and the IRS on a 1099-MISC Form. You will be required to list the amount reported on the 1099-MISC Form as income on your Federal and State tax returns. We will send you the 1099-MISC Form in January or February of the next year. The amount reported on the 1099-MISC Form will NOT include monies you received as a reimbursement for costs you incurred related to participating in this study. For example, reimbursements for parking or for drug co-pays will not be reported to the IRS or listed on the 1099-MISC Form.

Protecting data confidentiality

All research projects carry some risk that information about you may become known to people outside of the study. In order to minimize this risk, your name and other identifying information will be kept private. Your information used for the study will be labeled with a unique number and special code to keep them private. The unique number and code cannot be linked to your name except at the clinical center where you complete visits. Data from study visits labeled with the study ID will be sent to the Coordinating Center located at The Johns Hopkins University in Baltimore, Maryland. Some or all of the images taken of your eyes will be sent to the Photograph Reading Center located at the University of Wisconsin in Madison, Wisconsin. These images also will be identified only by your study ID. People at Johns Hopkins University, the National Eye Institute, the Food and Drug Administration (FDA), and the Institutional Review Board at this clinic may see the data collected about you during the study and review your records. These people work on the study and/or need to make sure the study is being done correctly. They may see your name and other identifying information as part of their review. However, they also must keep this information private.

People at AbbVie may see data collected from you that has to do with reports of possible side-effects of the drugs. AbbVie is the company donating adalimumab for the study.

Study data may be made available to other researchers. Results from this study may be published in medical journals. In both cases, your name or other identifying information will not be released to other researchers or medical journals.

By joining this study, you give permission for the study doctor or staff to contact you in the future about how you are doing or about other research studies. You do not have to join any other studies unless you want to.

Let us know if you have another doctor with whom you would like us to share the results of your study tests. We will share the test results with your other doctor if you give us your permission.

Certificate of Confidentiality protections

Your study information is covered by Certificate of Confidentiality protections. This allows us, in some cases, to refuse to give out your information without your permission even if requested using legal means. It does not protect information that we have to report by law, such as child abuse or some infectious diseases. It does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Alternatives to procedures or treatments

All of the study treatments are standard treatments for uveitis. They are all available outside of the study. Also, there are other treatments for uveitis that you could receive outside of this study.

Cost of participation in the study

Medical Care

You and/or your insurance will be charged for the regular medical care you need, in the same manner as if you were not part of this study. You will be responsible for costs not covered by insurance (for example, co-payments) for regular medical procedures and non-study treatments for uveitis just as you would be if you were not in the study.

Drugs that are prescribed to you as your assigned study treatment

Adalimumab

If you are assigned to receive adalimumab, the study will provide adalimumab to you at no cost for the time you are in the study. The maker of adalimumab, AbbVie, is donating the drug to the study. If a conventional immunosuppressive drug is added as part of your study treatment you will need to use your insurance coverage to cover the cost of the drug. The study will reimburse you up to $1500 for your out of pocket expenses for the drug.

Conventional immunosuppressive drugs
If you are assigned to conventional immunosuppression, you will need to use your insurance coverage to cover the cost of the drug or drugs. The study will reimburse you up to $3000 for your out of pocket expenses for these drugs.

You may need to provide receipts or other proof of your out-of-pocket cost to receive reimbursement. [Clinic provide details if required.]

Study procedures

Most of the procedures done in this study are standard procedures done as part of usual care for uveitis. Costs of standard procedures that are part of usual care will be billed to your health insurance and you may be responsible for co-pays depending on your insurance. This is done according to the policy of the National Institutes of Health, the government agency paying for this study.

Costs of procedures done only for the study are paid for by the study. For example, the study will pay for an MRI for patients with certain types of intermediate uveitis. This study is being conducted at many different clinics and includes patients with different kinds of uveitis. This will result in some differences in what procedures are done as usual care for a particular participant. If some procedures are required for the study more often than would be done for your usual clinical care, these extra procedures may be charged to the study.

What happens if you leave the study early?

You can agree to be in the study now and change your mind later. If you wish to stop participating in the study, please tell us right away. Leaving this study early will not stop you from getting regular medical care from this doctor and at this center.

If you leave the study early we will:

- Use and share the information and images of your eyes collected up to that time unless you contact [*insert name of the site's Principal Investigator*] to cancel or change your permission. Instructions to cancel or change your permission for use and sharing of your information and images are included in the Authorization for Disclosure of Protected Health Information for Research section of this consent form.

- Ask you if we can contact you to find out about your health and give you new information that we learn during the study, including the results of the study.
- Ask you for permission to collect information about your eye condition and health from your clinic visits for the study. We would get the information from your electronic medical record until the time that you would have completed the study, which is one year after you enrolled in the study.

Your study doctor may take you out of this study if staying in the study would be harmful to you or if you fail to follow instructions. The sponsor or regulatory agencies may stop this study at any time without your consent. If this happens, you will be notified and your study doctor will discuss other options with you.

How will I get my treatment after the study is over?

If you are doing well on your study treatment, you may want to continue it after you have completed the study. All of the study treatments are available outside of the study. If you are assigned to adalimumab, we will provide it to you for free during the study. If you want to continue adalimumab after you complete the study, you should check with your insurance to see if it covers this drug. AbbVie, the company that makes adalimumab, has a patient assistance program that might help you get the drug if you cannot otherwise afford it.

Conflict of Interest

A conflict of interest occurs when a researcher or the University has a financial or other interest that might affect the researcher's judgment when conducting a research study. In some situations, the results of a study might lead to a financial gain for the investigator(s) and/or [Johns Hopkins]. All such conflicts must be disclosed to the Conflict of Interest Committee. At this time, [Johns Hopkins University] is unaware of any potential conflicts of interest with regard to this research study.

Payment of treatment costs for injury or illness from study participation

If you are hurt or become ill as a result of being in this study, contact your study doctor immediately. Your study doctor will arrange for short-term emergency care or referral if it is needed. However, neither [Johns Hopkins University] nor the NIH have insurance plans that will pay you if you are hurt or have other bad results. Costs of such treatment may be billed to you or your insurance. Your health insurance may or may not pay for treatment of injuries as a result of your participation in this study. You do not waive any of your legal rights or release anyone from liability for negligence by signing this document.

Study Results

The purpose of this study is to determine which treatment is better for treating uveitis. Once the study is over, we will try to contact you to let you know the major conclusion(s) of this study. If your contact information has changed, this information may not reach you. However, according to National Institutes of Health policy, study results must be published on ClinicalTrials.gov.

Clinical Trial Registration

A description of this clinical trial is available on http://www.ClinicalTrials.gov, as required by the National Institutes of Health policy. The study registration number is NCT03828019. 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.

Authorization for Disclosure of Protected Health Information for Research

The Health Care Providers listed above are required by the Federal Privacy Rule to protect your private health information. By signing this Authorization, you permit them to release your information to the researchers for use in this research study. The researchers will try to make sure that everyone who needs to see your private information for this research keeps it confidential, but we cannot guarantee this. Although the researchers may not be covered by the Federal Privacy Rule, they will make an effort to protect your information using the same standards.

Your private health information that will be used for this research includes things learned by the procedures described in this consent form. The research team at your clinic also will collect your name, address, phone number, and other information that can identify you and link you to the health information collected in the study. Your date of birth and other dates (for example dates of study visits and procedures) will be included in the information sent to the Coordinating Center but other identifiers such as your name or address will not. Some or all of the images of your eyes taken during the study will be sent to the Reading Center. These images will be labeled only with your study ID and the dates the images were taken.

After this study ends, the Coordinating Center and Reading Center will continue to store the data and images of your eyes collected from you and other participants during the study. These data and images may be used for future research in uveitis and other health topics.

Some other people may see your private health information outside of the research team. They may include the sponsor of the study, study safety monitors, government regulators, and legal compliance staff. All these people must also keep your information confidential.

You do not have to sign this Authorization, but if you do not you may not join the study. It is your choice. Your Authorization does not have an expiration date; it will continue as long as the research continues. You may change your mind and take back this Authorization at any time. You may revoke (cancel) your permission to use or disclose all or part of your information and/or images of your eyes by contacting [*the site Principal Investigator*] by phone or in writing. [*The Principle Investigator's*] information is listed in the next section of the consent form. If you contact [*the Principal Investigator*] by phone, you must follow-up with a written request that includes:

- The name of the study: Adalimumab vs. Conventional Immunosuppression for Corticosteroid-sparing for Uveitis (ADVISE) Trial
- Your contact information
- What type(s) of information you no longer wish to share: (1) information from study visits; (2) images of your eyes (3) both information and images

- For which purpose do you no longer wish to share: (1) for use in future research; (2) for use in the study; (3) for use in either future research or the study
- The date and your signature

Who do I call if I have questions or problems?

- Call the principal investigator, [*Janet Holbrook at 443-287-5791*], if you have questions, complaints, or get sick or injured as a result of being in this study, or want to cancel your permission to use and share your information and images for the study or for future research.
- Call or contact [*the Johns Hopkins Bloomberg School of Public Health IRB Office*] if you have questions about your rights as a study participant. Contact the IRB if you feel you have not been treated fairly or if you have other concerns. The IRB contact information is:

  Address: *Johns Hopkins Bloomberg School of Public Health*
  615 N. Wolfe Street, Suite E1100
  Baltimore, MD 21205
  Telephone: *410-955-3193*
  Toll Free: *1-888-262-3242*
  E-mail: *JHSPH.irboffice@jhu.edu*

What does your signature on this consent form mean?

Your signature (or thumbprint/mark) on this form means:

- You have been informed about this study's purpose, procedures, possible benefits and risks.
- You have been given the chance to ask questions before you sign.
- You have voluntarily agreed to be in this study.

_____
Print name of Adult Participant

_____ _____
Signature of Adult Participant Date

_____
Print name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

Give one copy to the participant and keep one copy in study records