CONSENT FORM TO TAKE PART IN A CLINICAL RESEARCH STUDY AND AUTHORIZATION TO USE AND DISCLOSE HEALTH INFORMATION

Study Title:	Intravitreal Aflibercept Injection for Radiation Retinopathy Trial (ARRT)
Study #:	ARRT
Sponsor:	*NIA*
Study Doctor:	Thomas M. Aaberg Jr., MD
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For California participants: Before you read this consent form, you should read a copy of the California Experimental Subject's Bill of Rights. Ask the study staff for a copy of this document if you haven't already received one.

If this form contains words or concepts you do not understand, please ask the study doctor or the study staff to explain. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

SUMMARY

- You are being asked to be in a research study.
- Your decision to be in this study is voluntary.
- If you decide to be in this study and then change your mind, you can leave the study at any time.
- You can leave the study at any time with no penalty to you, and you won't lose any benefits except for possible benefits having to do with this study.
- The research-related activities in this study are not standard medical care and should not replace your usual medical care from your regular doctor.
- If you decide to take part in this study, you will be in this study for up to 52 weeks.
- If you agree to be in this research study, your study and medical records will become part of this research. The Sponsor of this study (Amy C. Schefler, MD), the FDA or other government agencies, and other groups associated with the study may have direct access to your study and medical records.

More detailed information about this study is in this consent form. Please read it carefully and ask as many questions as you need to before you decide if you want to be in the study. You should not sign the form if you have any questions that have not been answered.

This form has been reviewed by Quorum Review, a group of people who review research studies to protect the rights and well-being of people who take part in research studies. Review by Quorum Review does not mean that the study is without risks.

If you decide to take part in this research study, you must sign and date this consent form. Before you have anything done for this research study, you must sign this consent form.

PURPOSE

You are being asked to participate in this research study because you have previously been treated with radiation therapy and have now been diagnosed with damage to the retina caused by exposure to radiation (radiation retinopathy) and have swelling in the back of your eye (macular edema) associated with this.

The purpose of this research study is to determine whether injections of a drug called aflibercept (Eylea) into the eye are safe and effective *in* treating the swelling in the back of the eye. There is currently no approved therapy for this diagnosis, although it has been reported that drugs similar to the one that participants will be given may be beneficial. We (the study doctor and study staff) therefore would like to investigate whether aflibercept (Eylea) would be a safe and effective option for macular edema associated with radiation.

The use of aflibercept (Eylea) in this study *is* considered investigational, which means that Aflibercept (Eylea) has not been approved by the U.S. Food and Drug Administration (FDA) for the use of treating macular edema associated with radiation. Aflibercept (Eylea) is approved by the FDA for the treatment of wet age-related macular degeneration (AMO) since November 2011, macular edema following Central Retinal Vein Occlusion (CRVO) since September 2012, Diabetic Macular Edema (DME) since July 2014, and macular edema following RVO which includes CRVO and Branch Retinal Vein Occlusion (BRVO) since October 2014 .

To be eligible to participate in the research study you need to:

- read this entire document,
- understand the information within this document,
- if you decide you want to take part in this study, sign this document.

You should take part in this study only if you want to.

If you sign this document, a copy will be given to you and you can participate in the study as long as you meet all the study eligibility criteria. However, even *if* you sign this document, there is a chance that you may not be able to participate in the study (for example, if the study enrollment is complete, if you have a health condition that is not allowed in the study, etc.).

Be aware that this form refers to aflibercept (Eylea) as "study drug."

YOUR ROLE IN THE STUDY

Taking part in a research study can be an inconvenience to your daily life. Please consider the time commitments and responsibilities as a research participant when you are deciding whether to take part or not. Your responsibilities as a research participant include the following:

- Tell the truth about your medical history and current conditions.
- Tell the study doctor about any medications that you are currently taking, particularly for your eyes.
- Tell the study doctor if you have ever been in a research study involving the study eye (the eye that will receive study drug) or if you are in another research study now.
- Tell the study doctor about any problems you have during the study or if you have a change in address or phone number.
- Complete all study visits and procedures.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 men and women 18 years of age or older will participate in this study.

DURATION

Your participation in this study will last up to 52 weeks with up to 13 visits.

If you leave the study early, you would be asked to have the tests done that would happen at week 52.

PROCEDURES

If you are interested in participating in this study after it has been explained to you, you will be asked to come to the study center for a Screening Visit to see if you are eligible to participate in this study. You will sign this consent form at the very beginning of your screening visit before any study-related procedures are performed.

If the study doctor decides you meet the criteria (requirements) to be in this study, you will be assigned by chance (like flipping a coin) to one of two groups. You have an equal chance of being in one of these two groups:

1. **Group 1:** 15 participants will receive 3 doses of 2mg intravitreal (into the eye) aflibercept injections administered at screening/baseline, week 4, and week 8. At week 12 a follow-up visit will occur and if certain extension criteria are met, the participant will be injected with aflibercept and visits will be extended by 2 weeks. Participants could receive study drug at all visits except for the last visit (Week 52).
2. **Group 2:** Participants will receive 2mg intravitreal aflibercept injection at screening/baseline followed by a visit at week **4.** At week **4,** if certain extension criteria are met, the participant will be injected with aflibercept and visits will be extended by 2 weeks. Participants could receive study drug at all visits except for the last visit (Week 52).

You will not be able to choose which group you are in.

You will receive study drug in one eye (the "study eye").

If you decide to be in this study, you might have to stop using anti-VEGF injections in your other eye. The study doctor will tell you more about this.

Screening

At the Screening Visit, the study staff will ask you about your medical history and any medications that you have recently taken or are currently taking.

During the Screening Visit, you will have your vision and the tissues at the back of your eye (the retina) tested. These tests include the following:

- **Collecting your Medical and Ocular History**
  You will be asked some questions about your health and eye disease at your first visit. At each visit, you will also be asked about medicines you are using now and have used in the past. You will also be asked about any changes in your eyes and health at each visit.
- **Demographic Questions**
  You will be asked to give personal information, such as your date of birth, race, gender, etc. Your height and weight will be recorded. This will be done at the first visit only.
- **Vital Signs**
  Your blood pressure and heart rate will be taken at the first visit only.
- **Visual Acuity**
  Your study doctor or study staff will ask you to read letters on a chart to measure your vision. This will be done at every visit.
- **Dilated Slit Lamp Biomicroscopy**
  For this test, you will be given an eye drop of numbing medication. You will then be given other eye drops to dilate your pupils so that the study doctor can examine your eye. The study doctor will use a special lens and a bright light to look at the back of your eye. Your vision may be more blurred than usual for a while after this test. If you were able to drive before we carried out the test, you may not be able to do so for several hours afterwards. This will occur at every visit.
- **Intraocular Pressure (IOP) Assessment**
  This exam measures the amount of pressure inside your eyes. This test will be done after you have been given a drop of a medicine to numb your eyes so that you won't feel it. In order to check the pressure in your eye, this special instrument will come in contact with your eye for a few seconds. This test might be uncomfortable. This will occur at every visit.
- **Optical Coherence Tomography (OCT)**
  This test is a non-invasive (does not involve puncturing the skin) imaging test that uses light waves to take cross-section pictures of your retina. It allows the study doctor to measure the thickness of your retina and measure any macular edema. This test will be done at every visit, if applicable.
- **Optical Coherence Tomography Angiography (OCT-A)**
  This test is a non-invasive (does not involve puncturing the skin) imaging test that uses a very thin laser beam to create a picture of the tissue at the back of your eye. This test will be done screening/baseline, week 26, week 52, and Early Termination.

- **Fluorescein Angiogram**
  This test allows the study doctor to examine the blood vessels in your eyes. Your study doctor or study staff will inject a special dye (fluorescein) into a vein in your arm or hand and take eye pictures as the dye passes through blood vessels in your eyes. This test will be done on both eyes at screening/baseline, week 26, week 52, and Early Termination.
- **Fundus Photographs**
  This test allows the study doctor to examine the back of the eyes (fundus). These photos will be taken at screening/baseline, week 26, week 52, and Early Termination.
- **Pregnancy Test**
  If you are a woman who could get pregnant, a urine pregnancy test will be done at screening/baseline visit. The study doctor or study staff will tell you if the pregnancy test results are positive. Pregnant women cannot participate in the study. Ask the study doctor or study staff about how long they will store your urine sample.

If you are eligible to continue in the study, you will receive your first intravitreal injection (direct injection into the eye) of the study drug, aflibercept, in the study eye on your screening/baseline visit.

Before the injections are done, you will be given a local anesthetic so that your eye is temporarily numb in order to minimize pain. The anesthetic will be given either as eye drops, as an injection (subconjunctival anesthesia) into the clear tissue (conjunctiva) that covers the white part (sclera) of your eye, or both. The study doctor will explain the risks of the local anesthetic to you.

Will I need time to recover after my participation in the study?

Ask the study doctor or study staff for the estimated recovery time of your participation in this study.

Study Visits During the Main Part of the Study

You will be asked to return to the study center at least every 4 weeks. The study doctor or study staff will check your health and the medications you are taking. You will have many of the same exams you had during the Screening Visit, including:

- Eyesight testing at all visits
- Slit Lamp Examination at all visits
- Testing the pressure inside your eyes at all visits
- Fluorescein Angiography at Screening, week 26, and week 52 or Early Termination
- Fundus Photography at Screening, week 26, and week 52 or Early Termination
- Optical Coherence Tomography at all visits
- Optical Coherence Tomography-Angiography at Screening, week 26, and week 52 or Early Termination, if applicable

You could receive an intravitreal injection of 2mg aflibercept into your study eye at every study visit. We will ensure you can see out of your eye after the injection of the study drug and then you will be allowed to go home.

POTENTIAL RISKS TO YOU

There are potential risks to you by participating in this study, using aflibercept intravitreal injection into the eye, and having procedures performed as part of this study.

The Study Drug Used in This Study:

All drugs have side effects. Side effects are any undesirable and unintended effects of a drug or procedure. Not all side effects are known. Ask the study doctor if you have questions about the signs or symptoms of any side effects that you read about in this consent form. If you have any side *effects* or problems during your participation in the study, you should let your study doctor know right away, whether or not you think these problems are related to the study drug.

The following are known side effects of Aflibercept 2mg intraocular in jection:

- Intraocular inflammation (including endophthalmitis): The injection could cause inflammation or infection inside of the eye (endophthalmitis). This would need to be treated with medication and possibly surgery. This type of inflammation or infection is usually painful and could result in permanent loss of vision. In studies looking at injections into the eye, the chances of getting this kind of inflammation or infection ranged from 1 to 15 out of every 5,000 injections.
- Retinal tear/detachment: The injection needle could cause the retina, or other layers in the back of the eye, to tear and become detached from the eye (a retinal detachment). This could harm your vision and may require treatment.
- Traumatic cataract (sudden clouding of the lens of the eye): The injection needle could touch the lens in your eye during the procedure and cause a cataract (a condition in which the lens in your eye gets cloudy so that it is hard to see clearly).
- Arterial thromboembolic events (ATEs): ATEs are caused by blood clots forming in blood vessels in the body and may be associated with the family of drugs that block VEGF (Vascular Endothelial Growth Factor), including aflibercept. ATEs include events such as strokes and heart attacks; these events may be life-threatening or fatal.
- Embryo fetal toxicity: See the *"What happens if my partner or I get pregnant?"* section of this form.
- Immunogenicity: It is possible for your body to develop antibodies (proteins that protect you from infection or foreign substances) to the study drug. It is not known what the effect of these antibodies might be, but it is possible that they would block the study drug and prevent it from being effective. It is possible that antibodies may act against the body and cause you to become ill. The exact type of illness which could result from these kinds of reactions, and how serious the illness may be, cannot be predicted
- Hypersensitivity and Allergic Reaction: There is a chance that you may experience an allergic reaction to the study drug or anesthetic. Some people were noted to have had allergic reactions (also known as hypersensitivity) after receiving aflibercept into the eye. A severe allergic reaction would require immediate medical treatment and could result in permanent disability or death. If you believe you are having a severe allergic reaction, you should seek emergency medical treatment immediately and alert the study doctor

and study staff as soon as possible. Some signs that you may be having an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Sudden change in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat, or eyes
- Fast pulse
- Sweating

More information on allergic reactions appears below.

In prior clinical studies, Aflibercept has been injected into the eyes of participants with wet age-related macular degeneration (AM O), DME , macular edema following retinal vein occlusion (RVO), and myopic choroidal neovascularization (CNV). The following is a list of side effects from studies with Aflibercept that could have been caused by Aflibercept or by the injection procedure. An injection with a needle into the eye can be associated with damage to the eye and vision loss.

You might not experience any of these side effects. Always discuss any suspected side effects with your study doctor or the study staff.

Very Common Side Effects *(more than 1 in 10 participants may be affected):*

- decreased sharpness of vision (retinal pigment epithelium tear, detachment of the retinal pigment epithelium)
- certain forms of clouding of the lens (cataract, cataract cortical, cataract nuclear, cataract subcapsular)
- damage to the front layer of the eyeball (corneal erosion, corneal abrasion, punctate keratitis)
- increase in eye pressure (intraocular pressure increased)
- blurred vision
- moving spots in vision (vitreous floaters)
- detachment of the gel-like substance inside the eye from the retina (vitreous detachment)
- injection site pain
- a feeling of having something in the eye (foreign body sensation)
- increased tear production (lacrimation increased)
- swelling of the eyelid (eyelid edema)
- bleeding at the injection site (injection site hemorrhage)
- redness of the eye (conjunctiva hyperemia, ocular hyperemia)

Uncommon Side Effects *(between 1 and 10 in every 1,000 participants may be affected):*

- decreased sharpness of vision (retinal detachment, retinal tear)
- generalized allergic reactions (hypersensitivity)
- inflammation of certain parts of the eye (iridocyclitis, anterior chamber flare, iritis, uveitis)

- clouding of the lens (lenticular opacities)
- damage of the front layer of the eyeball (corneal epithelium defect)
- swelling of the front layer of the eyeball (corneal edema)

Rare Side Effects *(less than 1 in every 1,000 participants may be affected):*

- inflammation of the clear gel that fills the back of the eye (vitritis)
- pus in the eye (hypopyon)
- traumatic cataract

An injection of an anesthetic (xylocaine) into the membrane that lines the exposed portion of the eyeball and inner surface of the eyelids (subconjunctival) will be given as part of the injection procedure. Side effects associated with use of anesthetic subconjunctival injection include:

- eye pain
- bleeding at the injection site (subconjunctival hemorrhage)
- infection
- irregularity or swelling of the cornea

Unforeseeable Side Effects

It is possible that there will be other side effects associated with aflibercept which are unknown at this time, some of which may be serious or life-threatening.

Ask the study doctor about the risks of any medications you receive during this study.

Risk of Eye Examination including Slit-Lamp Examination and Dilation

Your pupils will be required to be dilated for multiple procedures during your study visit. The drops used to dilate your pupils may blur your vision, cause a slight burning sensation, and make you sensitive to light. The dilating effects of the drops will wear off after several hours. Due to this, you will be advised to have someone accompany you to all study visits to drive you home after the exam is complete.

In rare cases, the use of numbing eye drops may cause an allergic reaction, difficulty in breathing or low blood pressure. You must tell the study doctor if you are allergic to numbing eye drops.

Risks of Testing the Pressure Inside Your Eye

The instrument used to measure the pressure inside your eye could cause a corneal abrasion (scratch on the clear front surface of your eye). If this occurs, it will be treated by your study doctor.

Risk of Optical Coherence Tomography (OCT)

The optical coherence tomography uses bright light to take photos of your retina. As with any bright light source, some people may experience sensitivity to light for a short time.

Risk of Optical Coherence Tomography-Angiography (OCT-A)

There are no known risks from this test. Your eye will be exposed to light levels which are lower than those used routinely in an eye examination, and are considered safe. Holding your eye open for the time required to take images may be uncomfortable.

Risk of Fundus Photography (FP)

During the FP, you may have some brief discomfort and you may "see spots" for a few minutes after the pictures are taken.

Risk of Fluorescein Angiography

Fluorescein angiography risks may include:

- bleeding and bruising on the skin of the arm around the needle stick
- itching , rash, or vomiting

Mild reactions such as itching, swelling, or redness near where the dye is put in your vein are more common and have been estimated to happen in 1 out of 100 times.

Rare, severe allergic reactions can also happen during the test:

- Serious allergic reactions such as severe swelling and difficulty breathing can happen in 1 out of 10,000 people.
- About 1 out of 222,000 people may have a heart attack, stroke (blood clots in the brain), or even die from fluorescein dye administration.
- If you have ever had a severe allergic reaction to fluorescein dye administration, you cannot be in the study. A severe allergic reaction would require immediate medical treatment and could result in permanent disability or death.

During the fluorescein angiography, you will be closely monitored. If you develop an allergy, you will be treated according to your study doctor's judgement. You should tell your study doctor or a member of the study staff about any new health problems that develop while you are in this study and about any new medications you start taking (including over-the-counter medication, herbal remedies, and non-prescription drugs).

If you experience any side effects during the course of this study, you should immediately contact the study doctor or the study staff.

Allergic Reactions

Sometimes people have allergic reactions to drugs (including anesthetic and fluorescein dye). If you have a very bad allergic reaction , you could die. Some things that happen during an

allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- shortness of breath
- wheezing
- difficulty breathing/inability to breathe without assistance
- tightness in the throat
- rash
- hives
- tingling
- swelling of the face, eyes, and mouth
- swelling of the throat
- dizziness
- a sudden drop in blood pressure
- fast pulse
- sweating
- a feeling of dread
- other symptoms as explained by study personnel

IF YOU BELIEVE YOU ARE SUFFERING FROM AN ALLERGIC REACTION, IMMEDIATELY CALL AN EMERGENCY HOT LINE TO RECEIVE MEDICAL CARE.

Other Risks

It is possible that receiving Aflibercept may change how your regular medications, vaccines, or supplements work. It is very important that you tell the study doctor about any medications, supplements, or vaccines before you take them during the study.

If you stop any of your regular medications to be in the study, your eye health might get worse. Please tell the study doctor or study staff right away if you have any problems when you stop or change your regular medication.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

WHAT HAPPENS IF MY PARTNER OR I GET PREGNANT?

Women who can get pregnant or are breastfeeding:

Women who are currently pregnant or breastfeeding may not take part in this research study. If you are female, you must not be pregnant or become pregnant during this study. The study drug has not yet been tested in pregnant or nursing women; there may be unknown risks to you, the unborn child, or nursing child.

You must agree to use a medically acceptable method of birth control prior to the first dose of the study drug until 3 months after the last dose of study drug. Please discuss acceptable birth control measures with your study doctor.

If you become pregnant, you may no longer participate in this study. If you become pregnant within 3 months of the last dose of study drug:

- You must tell the study doctor immediately.
- Your study doctor will ask to follow-up with you on the outcome of the pregnancy as required by the study plan. The study doctor or study staff may share information about the pregnancy with Regeneron Pharmaceuticals, Inc., a company that awarded the sponsor (Dr. Amy C. Schefler) to conduct this research study.

Men:

If you are a man taking part in this study, there may be risks to an unborn child that you father during or after the study. Nobody knows what all the risks are right now. Please discuss acceptable birth control measures with your study doctor.

You must agree to use a medically acceptable method of birth control prior to the first dose of study drug until 3 months after the last dose of study drug unless your partner cannot become pregnant (such as sterile partner, etc.).

If your partner becomes pregnant during your participation in the study or within 3 months of your last dose of study drug:

- You must tell the study doctor immediately.
- With your partner's written permission, your study doctor will follow-up with your partner on the outcome of the pregnancy as required by the study plan. The study doctor or study staff may share information about the pregnancy with Regeneron Pharmaceuticals, Inc.

If you experience a side effect during this study

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

If you experience a dangerous or life-threatening reaction, your study doctor may have to remove the study drug from your study eye through a surgical procedure called vitrectomy. Should this happen, you will be given explanations about the vitrectomy surgery and will have to sign a separate consent form for this procedure.

It is very important that you report to the study doctor and the study staff about any side effect you may experience.

POTENTIAL BENEFITS

Your vision may stabilize or may improve while you are in this study; however, this cannot be assured. Your vision may get worse while you are in this study. The results of this study may help researchers to better understand radiation retinopathy and help others in the future.

ALTERNATIVES TO STUDY PARTICIPATION

You do not have to be in this study to receive help for your eye condition. There is currently no approved therapy for your diagnosis, but you may choose to receive:

- intravitreal injections of anti-VEGF medications
- intravitreal injections of steroids
- laser treatment

Before you decide whether or not to be in this study, your study doctor will discuss the other options that are available to you, including their risks and benefits. In addition, you may discuss your options with your regular health care provider.

CONFIDENTIALITY OF PERSONAL INFORMATION

Records created by a doctor or hospital, as part of medical care, are called medical records. Records created by a research study are called research records. The records that will be collected, used, and shared for this study may include your research records and supporting information from your medical records, such as:

- Name
- Address
- Telephone number
- Birth date
- Race
- Sex
- Allergies
- Medications you take (current and past)
- Your past medical history including medical information from your primary care physician
- Physical exam, laboratory tests (blood and urine)
- Response to any study drug or study procedures you receive
- Information related to study visits and phone calls
- Other tests or procedures that may be performed
- Other medical information relating to your participation in this study

This information may be seen by the Sponsor, representatives of the Sponsor, Quorum Review, the FDA, and any appropriate government agencies. Your records that identify you will be protected as required by law and according to any policies the study center or sponsor may have. However, absolute confidentiality cannot be promised because information needs to be shared. After its release, information that can identify you may no longer be protected by federal privacy rules.

Your urine sample will not be labeled with your name or other directly identifying information. Your sample will have a code instead. The list that matches the code with your name will be stored separately from your sample.

CLINICALTRIALS.GOV

A description of this clinical trial will be available on *http://www.Clinica/Trials.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.

PAYMENT FOR INJURY

If you think you have been injured as a result of participating in the study:

- Promptly seek medical treatment, and
- Call the number(s) on the first page of this form.

Your insurance will be billed for this treatment in the ordinary manner. No other payment is routinely available from the study doctor or sponsor. To ask questions about this, talk to the study doctor or study staff.

You do not waive (give up) any of your legal rights or release anyone from liability for negligence by signing this document.

Be aware that your health care payer/insurer might not cover the costs of study-related injuries or illnesses.

PAYMENTS TO YOU

You will not get paid for being in this study.

WHO IS PAYING FOR THIS STUDY?

Regeneron Pharmaceuticals , Inc. awarded Dr. Amy C. Scheffer , the sponsor of the study, money to conduct this research study. This means that Retina Consultants of Houston (where the sponsor works) is receiving payments from Regeneron Pharmaceuticals, Inc. to support the activities that are required to conduct the study.

VOLUNTARY PARTICIPATION

Your participation in this study is voluntary. You may refuse to participate or you may discontinue your participation at any time without affecting your continuing medical care or benefits to which you would otherwise be entitled. There will be no penalty to you. If you decide to withdraw, you should contact your study doctor. If you discontinue from the study, you will be asked to return for a final study visit.

The Sponsor, the study doctor or Quorum Review may discontinue the study or your individual participation in the study at any time without your consent for reasons including:

- your failure to follow directions
- it is discovered that you do not meet study requirements
- it is in your best interest medically
- the study is canceled

- administrative reasons

If you leave the study, the study doctor and study staff will still be able to use your information that they have already collected.

If you change your mind later, be aware that your urine sample may or may not be withdrawn from the research, depending on the sponsor's policies. You can ask the study doctor or study staff about this.

COSTS TO YOU

The sponsor, Amy C. Schefler, MD will provide the study drug, clinic visits, anesthetic (numbing) eye medicine, and tests related to the study at no charge during this study.

You or your insurance company may be billed for any standard medical care given during this research study (for example any care given to the non-study eye).

Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include the costs of treating side effects. Otherwise, you might have unexpected expenses from being in this study.

Before you agree to be in this study, you should talk with your health care payer/insurance company about its payment policy for covering standard medical care given during a research study and the costs required as part of your participation. If your insurance company does not pay, you may be billed for some procedures or medications.

YOUR RESPONSIBILITIES

When deciding whether to participate, consider whether you are able and willing:

- To commit the time required to keep appointments
- To tell the study doctor truthfully about your complete medical history
- To report any new medical problems, illnesses, or changes in your medication or health during the study
- Women of childbearing potential and men with partners of childbearing potential must use an acceptable method of birth control until 3 months after the last dose of study drug. Your study doctor will discuss this with you in more detail.

You should tell the study doctor or study staff if you want to stop being in the study at any time.

NEW FINDINGS

You will be informed in a timely manner of any new findings that may influence your willingness to participate or to continue participation in the study.

GETTING ANSWERS TO YOUR QUESTIONS ABOUT THE STUDY

In the event of an emergency, dial 911 immediately.

If you require emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor or study staff as soon as possible.

You can ask questions about the study at any time. You can call the study doctor or study staff at any time if you have any concerns or complaints. You should call the study doctor or study staff at the phone number listed on page 1 of this form if you have questions about the study procedures , study costs (if any), study payment (if any), or if you get hurt or sick during the study.

Quorum Review reviewed this study. Quorum Review is a group of people who review research studies to protect the rights and welfare of research participants. Review by Quorum Review does not mean that the study is without risks. If you have questions about your rights as a research participant, if you are not able to resolve your concerns with the study doctor or study staff, if you have a complaint, or if you have general questions about what it means to be in a research study, you can call Quorum Review or visit the Quorum Review website at www.quorumreview.com.

Quorum Review is located in Seattle, Washington.
Office hours are 8:00 AM to 5:00 PM Pacific Time, Monday through Friday.
Ask to speak with a Research Participant Liaison at 888-776-9115 (toll free).

CONSENT

I have read and I understand this consent form, and I have had the opportunity to ask questions prior to undergoing any study related testing. All of my questions were answered satisfactorily.

I know that at any time I may ask other questions. I have had ample time to consider whether to participate in this study.

I voluntarily agree to participate in this study. I understand that I will be given a copy of this consent form after it is signed. I agree to follow the study doctor's instructions.

By signing this form, I have not given up any legal rights I have as a research subject.

Richard Thompson
ıted Name of Participant
Printed Name of Participant

Richard V Thompson
ıature of Participant
Signature of Participant

1/23/18
te

I attest that the individual providing consent had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation in this study.

Holly Vincent
ne of Person Explaining Con
Printed Name of Person Explaining Consent

Holly Vincent
Signature of Person Explaining Consent

23-Jan-2018
Date

AUTHORIZATION TO USE AND DISCLOSE HEALTH INFORMATION

Introduction

You are being asked to read, review, and sign this authorization agreement as a result of a federal law on the privacy of identifiable health information. The law is called the Health Insurance Portability and Accountability Act (HIPAA). It requires that research subjects receive written notification about the collection, use and disclosure (sharing) of health information that can identify them. In addition, it requires researchers (like the study doctor) to ask research subjects for permission to use and disclose identifiable health information for the purpose of this research study.

Signing this authorization agreement authorizes the study doctor and study staff to collect health information that can identify you and to use and disclose this information to the parties specifically named in this authorization agreement.

Explanation of Authorization

Information used and disclosed may include your name, address, telephone number, research records, supporting information from your medical records, results of laboratory, diagnostic or other tests, and research observations made during your participation in the research study.

As part of this study, the study doctor and staff will record health information about you that contains your name and other items that can be used to identify you. The health information that will be collected from you if you participate in the study includes:

- Information obtained from procedures to determine your eligibility to participate in the study, including a routine medical history and tests required by the study.
- Information that is created or collected from you during your participation in the study, including results of any tests and procedures performed during the study.
- Information contained in your underlying medical records related to your medical history and treatment.

In most cases, the study doctor will assign a code number to your information that is shared with the Sponsor. The Sponsor, Dr. Amy C. Schefler, her representatives, and others involved in this study (including Regeneron Pharmaceuticals, Inc.) may review or copy your protected health information at the study site to check the safety and results of the study. Regulatory authorities and Quorum Review may also review or copy your information to make sure that the study is done properly or for other purposes required by law.

Authorized representatives of the sponsor, Regeneron Pharmaceuticals, Inc., Quorum Review, the FDA and other U.S. governmental agencies, and possibly governmental agencies of other countries will be given access to these records on request and may copy them. Copies of the study records that do not include your name but may be traced back to you may be given to Quorum Review and laboratories working with the Sponsor on this study. The Sponsor may send a copy of the records to the FDA or other regulatory agencies such as governmental agencies in other countries. By signing this form you are authorizing this use and disclosure which also includes electronic health information.

Because of the need to release information to these and other parties, absolute confidentiality cannot be guaranteed. Once your information is disclosed to the study sponsor, its agents, Quorum Review, or government agencies as described above, there is potential that your medical information will be re-disclosed and may no longer be protected by federal privacy rules. However, information will be collected and shared following professional standards of confidentialtiy.

This Authorization is valid once it is signed and dated by you. If you do not withdraw this Authorization in writing, it will expire December 31, 2050. Your study doctor will keep this Authorization for at least 6 years.

Information and results from this study may be presented at meetings or published in journals. Your name, and information that can easily be traced back to you, will not be included in presentations and publications.

Suspension of Your Right to Access Personal Information

Your research records may be used to make health care decisions about you. Under federal privacy rules you have a right to inspect and obtain a copy of your protected health information, including protected health information maintained in the study records. However, the right to inspect and obtain your protected health information in the study records may be suspended during the study to keep from spoiling the study results.

If there is a medical need during your participation, study records may be made available to medical professionals who are caring for you, as needed for your care.

Voluntary Participation

Your authorization to use and disclose your identifiable health information for the purpose of this research study is voluntary. However, if you do not provide your written authorization for the use and disclosure of your identifiable health information, you cannot participate in this research study.

In addition, your participation in the overall research study is entirely voluntary. You may refuse to participate or may quit at any time during the study. All you have to do is tell the study doctor.

If you decide to stop participating in the research study, you may also end your authorization allowing the researchers to collect, use and disclose any additional health information that could identify you. To end your authorization, you must notify the study doctor of your decision in writing. If you cancel your authorization, you will not be able to continue in the study. Send your written withdrawal notice to the study doctor at the address on page 1 of this form.

If you end your authorization, no new health information that can identify you will be gathered from you or your existing medical records. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor. Information that is in your study records at the time that your authorization is ended cannot be removed. Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

If you withdraw from the study but do not withdraw your Authorization, new protected health information may be collected until this study ends.

You may freely ask questions about this authorization agreement now or at any time. If anything causes you concern, or you have questions, you may contact the study doctor or study staff at the telephone number printed on the first page of this form.

STATEMENT OF AUTHORIZATION

I have read this authorization agreement and its contents were explained. My questions have been answered. I voluntarily authorize the study staff to collect, use and disclose my health information as specified in this authorization agreement. I will receive a signed and dated copy of this authorization form for my records. By signing this authorization form, I am not giving up any of my legal rights.

Wendy Thompson
gnature of Participant _____ ; jg3 f; c9
date 7

STATEMENT OF PERSON EXPLAINING AUTHORIZATION

I have carefully explained to the subject the nature and purpose of the authorization agreement. I have been available to answer any questions that the subject has regarding this authorization agreement.

Holly Vincent
_____ Person Explaining Au

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