Clinical Study Protocol

Prevention Of Macular Edema In Patients With Diabetic Retinopathy Undergoing Cataract Surgery

NCT01988246

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Cleveland Clinic
Consent to Participate in a Research Study

Study Title: **Pr**evention **O**f **M**acular Edema **I**n Patients With Diabetic Retinopathy Undergoing Cataract **S**urg**e**ry (PROMISE Study)

Principal Investigator: Rishi Singh, M.D.

Sponsor: Regeneron/Bayer Pharmaceuticals, Inc.

Carefully review this consent document. The purpose of a consent document is to provide you with information to help you decide whether you wish to participate in research. Your decision is completely voluntary and will not affect your medical care if you choose not to participate. It is important for you to ask questions and understand the research risks, benefits and alternatives.

Please note:

- **You are being asked to participate in a research study**
- **Carefully consider the risks, benefits and alternatives of the research**
- **Your decision to participate is completely voluntary**

Your doctor may be an investigator in this research study, and as a research investigator, is interested in both your welfare and in the conduct of the research study. Before entering this study or at any time during this research, you may ask for a second opinion about your care from another doctor who is not involved with the research study. You are not under any obligation to participate in any research project offered by your doctor.

Conflict of Interest Disclosure

One or more of the investigators conducting this study serve as paid speakers, consultants or advisory committee members for the company that is paying for this research or a company that makes products used in this study. These financial interests are within permissible limits established by the Cleveland Clinic Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask your study doctor or call the Institutional Review Board at 216-444-2924.

1. INFORMATION ON THE RESEARCH

Why Are You Being Asked To Take Part In This Research?

You are being asked to participate in this research study because you have a cataract which will require surgical removal and have Type 1 or Type 2 Diabetes.

Why Is This Study Being Done?

The purpose of this study is to evaluate the safety and efficacy of intravitreal Aflibercept (Eylea)

injection to sham injection in reducing the percentage of diabetic retinopathy participants who develop macular edema within 90 days after cataract surgery. For this study, the term “study drug” refers to Aflibercept (Eylea).

The Food and Drug Administration (FDA) has approved the use of Aflibercept for the treatment of wet age related macular degeneration and macular edema from central retinal vein occlusions. This use of Aflibercept® has not been approved by the Food and Drug Administration (FDA) and is therefore considered “investigational.”

A cataract is a clouding of the normally clear lens of your eye. Cataracts commonly affect distance vision and cause problems with glare. They generally don't cause irritation or pain. As the clouding progresses, the cataract eventually interferes with your vision and cataract surgery may be necessary.

Cataract development occurs at a higher rate and at an earlier age in diabetic patients compared to non-diabetic patients. Additionally, diabetic patients who have retinopathies (a condition that affects the nerves at the back of the eye) are more likely to develop a condition called macular edema after cataract surgery. Macular edema occurs when fluid collects within the tissues at the back of the eye and causes these tissues to swell. This is caused by the leakage of blood vessels within the retina. A potent mediator for blood vessel leakage is vascular endothelial growth factor (VEGF). Cystoid macular edema (CME) is a type of macular edema in which distinctive fluid-filled cysts are present. In many cases there may not be any noticeable changes, but central vision may change if the swelling affects the central portion of the retina (called the macula). Because the macula is the area of the retina that is used for reading, seeing fine details and color, preventing and treating macular edema are important goals for cataract surgeons.

After cataract surgery, doctors often prescribe steroid eye drops. Recent studies with other anti-vascular endothelial growth factor drugs suggests that using these drugs may reduce the incidence and severity of macular edema. In some cases, macular edema may not appear until weeks after surgery. Therefore, there is a need for well-controlled studies to show whether this medication can decrease the chance of developing macular edema for up to 90 days after cataract surgery.

How Many People Will Take Part In The Study?

About 30 people will take part in this study at the Cleveland Clinic.

What Is Involved In The Study?

If you agree to participate in this study, you will be assigned randomly (by chance, like the flip of a coin) to one of the two following investigational eye drop groups:

- A single eye injection of Aflibercept (Eylea) during the time of cataract surgery.

- Sham injection which will consist of pressing an empty needle against the eye wall without penetration.

Every participant has an equal chance of receiving either assignment. Neither you nor your study doctor will know to which group you have been assigned. This information is available in the event of a medical emergency.

All participants in the study will have their cataracts removed in the same manner, using their study doctor's standard surgical procedures and standard surgical equipment and medications. Additionally, your study doctor will prescribe Vigamox® (Moxifloxacin) eye drops, which you will use as one drop four times daily for the first 2 weeks following surgery. Your study doctor may ask you to continue using this steroid and antibiotic eye drop based on his or her medical judgment beyond 2 weeks following the surgery.

There is no experimental equipment involved in this study.

Your study doctor will examine your eyes during a screening visit to confirm that you do not have any condition(s) that would prevent you from participating in this clinical research study. Additionally, your eligibility for the study will be confirmed by Dr. Rishi SIngh based on the entry requirements set for all subjects by the sponsor of the research. If you meet the requirements of this clinical research study and you agree to participate, then you will be responsible for attending examinations as described below.

Baseline and Screening Visit: (-4 weeks to -2 days, 2 days to up to 4 weeks prior to scheduled surgery): Approximately 3 hours
The Screening visit and Baseline visit include tests that are performed separately by your cataract study doctor and by a retina (back of the eye) study doctor. The completion of these tests may occur on different days.

Before the research begins, you will be asked to read the consent document carefully. The study doctor or study staff will discuss the study with you and answer any questions you may have about the study. After all your questions have been answered and understand what is involved in the study, you will be asked to sign the consent document.

After the consent process is completed, the screening visit will begin. This will consist of the following:

- Ask if you have had any changes in your health or changes in any medications since the Screening Visit;
- Measure how well you can see (visual acuity). This test is painless and requires you to identify letters on a chart while you are standing at a distance away from the chart. The test will be scored by how many letters are identified correctly.
- Evaluate the health of the various parts of both eyes (cornea, front section of your eye, and your lens) by use of a "slit-lamp" microscope (an instrument used by your study doctor to look inside your eye). This eye test looks at the front of the eye by shining a beam of light shaped like a small slit on the eye. The eye doctor may also dilate your

pupils while you are undergoing this eye exam. The eye test can be used to help diagnose cataracts, retinal detachment, macular degeneration, injuries to the cornea and presbyopia.

- Measure the pressure inside both eyes (IOP) This is an eye test used to help diagnose glaucoma in which a small, smooth instrument known as a tonometer is lowered onto the surface of the eye in order to measure the pressure in the eye.
- Dilate both pupils to evaluate the health of the back section of your eyes.

Your cataract study doctor will explain the study to you and answer your questions.

If you are female, you will have a urine pregnancy test unless you have had a hysterectomy or are postmenopausal for at least 1 year. The test must be negative in order to participate in this study. This test is being performed for safety purposes and is not an investigational procedure.

The thickness and volume of your macula, the "yellow" oval spot near the center of the retina mainly responsible for your central vision, will be measured using optical coherence tomography (OCT) equipment. This test is painless, and is similar to having photographs taken of your eye using a slit-lamp camera (a slit lamp is a device that your eye doctor uses to look at your eyes while you are seated). You will be required to sit still during the brief scanning procedure (a few seconds) for each eye. The OCT scans take about 10 minutes altogether.

The study doctor will take photographs of the back of your eye, specifically the optic nerve, vitreous, macula, retina and its blood vessels. Before beginning, your pupil will be dilated using special eye drops.

Your fundus photographs, OCT images will be evaluated by Dr. Singh to determine the severity of your diabetic retinopathy and confirmation of your eligibility to participate in the study. In case your cataract is too dense to obtain good quality fundus photographs and Dr. Singh cannot determine the severity/eligibility in the study, your physician will confirm your severity/eligibility based on the exam of the back of the eye. If your severity/eligibility is confirmed by your physician at study entry, you will have to have a follow up fundus photograph taken during the Day 7 visit.

You will be informed of medications (steroids and non-steroidal anti-inflammatory drugs) that you should avoid using while participating in this study. If you are currently taking a steroid or non- steroidal anti-inflammatory medicine, please notify your eye study doctor. The retina study doctor will dilate the pupils of your eye with eye drops so that your retina can be seen. This will be done in order to evaluate any conditions in the back of your eye that may prevent you from participating in this study. The retina study doctor also will give a preliminary assessment of the severity of your diabetic retinopathy. You will have photos taken of the fundus of your eye (tissues in the back of your eye).

In addition to these procedures which are common for pre-surgery participants, a HbA1c lab test will be performed. This test helps estimate how well a person's diabetes has been controlled over the past 3 months. A small amount of blood (about ¼ teaspoon) is needed for this test,

taken either by a finger stick or blood draw. The Baseline Study Visit and the HbA1c lab test is paid for by the Sponsor. Any pre-admission testing ordered by your doctor, will be billed to your insurance carrier.

On the Day of Surgery (Day 0):
You will inform your study doctor or his/her technician of any changes in your health and/or medications since the preoperative examination.

Your study doctor will remove your cataract using his/her standard surgical procedure and standard equipment and implant an intraocular lens. Your study eye will be anesthetized (made numb) for the cataract procedure. The skin around your eye and the surface of the eye will be treated with an antiseptic solution (povidone iodine). Then, the doctor will inject the medication into your eye.

Your study doctor will replace your cataract with a standard intraocular lens in order to help improve your vision. You will be given a separate consent form as necessary for these standard procedures.

In addition to any other post surgery medications your study doctor may give you, you will be given Vigamox® to be used four-times-daily for two weeks following surgery.

You may use Tylenol® (acetaminophen) for any mild discomfort you may experience following surgery. You will be asked to only use Tylenol for mild pain or discomfort. If the Tylenol does not provide sufficient relief from pain or discomfort, you should contact your study doctor so that you may receive appropriate medical care, which may include 325 mg of aspirin or additional medication as decided by your study doctor.

Examination 1 Day Following Surgery (Day 1 visit): Approximately 1 hour

One day following your surgery your study doctor (and/or a technician) will:

- review your medications
- test how well you can see (visual acuity);
- evaluate the health of the various parts of your eye (cornea, front section of your eye, and your lens) by use of a “slit-lamp” microscope;
- measure the pressure inside your eye (IOP)

You should inform your study doctor of any changes in your health and/or medications since the previous day.

Examination 1 Week Following Surgery (Day 7 Visit): Approximately 2 hours

Approximately 7 days after your surgery, your study doctor (and/or a technician) will perform the

same examination as described above for the Day 1 Visit.

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye, and your lens) by use of a “slit-lamp” microscope.
- Measure the pressure inside your eye (IOP)

Additionally, optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula photograph will also be taken at this visit. If your severity of retinopathy and eligibility at study start was confirmed by your physician and not the Central Reading Center due to dense cataract, fundus photograph will also be taken at this visit.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

Examination 14 Days Following Surgery (Day 14 Visit): Approximately 2 hours

Approximately 14 days after your surgery, your study doctor (and/or a technician) will perform the same examination as described above for the Day 7 Visit.

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye and your lens) by use of a “slit-lamp” microscope.
- Measure the pressure inside your eye (IOP)

- A drop of fluorescein dye (a standard diagnostic eye drop) will be placed in your eye to assess the health of the cornea (the clear front part of the eye).

- Optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula.

Your study doctor will also assess any conditions that indicate you may need treatment that is different from the study drug. If necessary, you will be withdrawn from the study and be given appropriate treatment. You will remain in the study and complete all future follow-up visits.

The Vigamox® eye drops will be stopped at this visit, unless your study doctor requests that you continue using this medication.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

Examination 30 Days after Surgery (Day 30 Visit): Approximately 2 hours

Approximately thirty days after your surgery, your study doctor (and/or technician) will perform the same examination as described above for the Day 14 Examination.

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye and your lens) by use of a “slit-lamp” microscope.
- Measure the pressure inside your eye (IOP)
- Optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula.

Your study doctor will also assess any conditions that indicate you may need treatment that is different from the study drug. If necessary, you will be withdrawn from the study and be given appropriate treatment. You will remain in the study and complete all future follow-up visits.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

Examination 60 Days after Surgery (Day 60 Visit): Approximately 2 hours

Approximately sixty days after your surgery, your study doctor (and/or a technician) will perform the same examination as described above for the Day 14 Examination.

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye and your lens) by use of a “slit-lamp” microscope.
- Measure the pressure inside your eye (IOP)
- Optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula.

Your study doctor will also assess any conditions that indicate you may need treatment that is different from the study drug. If necessary, you will be withdrawn from the study and be given appropriate treatment.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

Examination 90 Days After Surgery (Day 90 Visit): Approximately 2 hours

Approximately ninety days after your surgery, your eye study doctor (and/or technician) will perform the same examination as described above for the Day 14 Examination.

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye and your lens) by use of a “slit-lamp” microscope.
- Measure the pressure inside your eye (IOP)

- Optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula.
- In addition to these procedures, a Dilated Fundus exam will be performed. You will also be asked to return the study eye drop medication bottles.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

Schedule of Events

Study Procedure	Baseline and Screening (-4 weeks to -2 days)	Day 0 **Surgery**	Day 1	Day 7 (± 2 days)	Day 14 (-1/+4 days)	Day 30 (±7 days)	Day 60 (±7 days)	Day 90/ Early Exit (± 7 days)
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**9**
Review Inclusion and Exclusions	X							
Sign informed consent	X							
Record demographics and history	X							
Randomization		X						
Review study medications	X	X	X	X	X	X	X	X
Vital Signs	X							X
Vision testing with ETDRS eye chart	X		X	X	X	X	X	X
Intraocular Pressure	X		X	X	X	X	X	X
SD-OCT	X		X	X	X	X	X	X
Dilated Fundus Exam	X							X
Wide-field fundus photography	X							X
Slit Lamp	X		X	X	X	X	X	X
Pregnancy test if applies	X							
Hemoglobin A1C value	X							
Administer Study Drug/Sham		X						

Early Discontinuation from the Study:
Your study doctor may withdraw you from the study at any time if it is determined in his/her best medical judgment that your continued participation is not in your best interest. Your study doctor also will assess any conditions that indicate you may need treatment that is that is different from the study drug. If necessary, you will be withdrawn from the study and be given appropriate treatment. You will remain in the study and complete all future follow-up visits.

You will inform your study doctor of any changes in your health and medications since the previous examination.

If you withdraw from the study at a visit date prior to the Day 90 visit, you will have the appropriate exam for that visit date, as well as all other tests specified:

- Your medications will be reviewed
- Test how well you can see (visual acuity)
- Evaluate the health of the various parts of your eye (cornea, front section of your eye and your lens) by use of a "slit-lamp" microscope (an instrument that projects a beam of light allowing the doctors to view the eye).
- Measure the pressure inside your eye (IOP)
- Dilated Fundus exam
- Optical coherence tomography (OCT) will be performed on your eye to assess the thickness and volume of your macula.

You should inform your study doctor of any changes in your health and/or medications since your last visit.

You also have the right to withdraw from the study at any time without penalty. This is discussed further in the section to follow called "VOLUNTARY PARTICIPATION/WITHDRAWAL".

How Long Will You Be In The Study?
Your participation in this study will last 90 days (+/- 7 days) after cataract surgery.

2. RISKS AND DISCOMFORTS

What Are The Risks Of The Study?

The most common side effects reported in clinical studies with the use of Aflibercept includes:

Table 1: Most Common Adverse Reactions (≥1%) in Phase 3

Adverse Reactions	EYLEA (N=1824)
Conjunctival hemorrhage	25%
Eye pain	9%
Cataract	7%
Vitreous detachment	6%
Vitreous floaters	6%

Adverse Reactions	EYLEA (N=1824)
Intraocular pressure increased	5%
Conjunctival hyperemia	4%
Corneal erosion	4%
Detachment of the retinal pigment epithelium	3%
Injection site pain	3%
Foreign body sensation in eyes	3%
Lacrimation increased	3%
Vision blurred	2%
Retinal pigment epithelium tear	2%
Injection site hemorrhage	1%
Eyelid edema	1%
Corneal edema	1%

There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence in the VIEW1 and VIEW2 wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA

As with any drug, it is possible that you could experience an allergic reaction to any of the drugs or combination of the drugs used in this study. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and–rarely–death. You will be monitored carefully after administration of the study drug for signs of an allergic reaction. There are trained medical personnel and emergency equipment and medicines available at the research center to treat you in the event of an allergic reaction. **If you think you are having a severe allergic reaction after you leave the study center, call an ambulance and seek medical attention immediately.**

Tylenol (acetaminophen) may be associated with stomach upset.

FLO-GLO® Fluorescein Sodium Sterile Ophthalmic Strip may, if used, cause eye irritation.

The risks of drawing blood from a vein or finger stick include discomfort at the site of the needle stick, possible bruising and swelling around the site of the needle stick, rarely an infection, and uncommonly feeling faint from the procedure.

For the eye examination, your pupil(s) will be dilated. Dilation of the pupil may cause light sensitivity and slight blurring of vision for up to 4 hours after testing. Wearing sunglasses for several hours after dilation can help reduce the discomfort of light sensitivity. Also, driving may be difficult so it is advisable to arrange for transportation home, particularly on the Baseline visit and the Day 90 visit when both eyes will be dilated.

There are risks associated with all surgeries including this type of surgery (cataract removal and intraocular lens implantation). These may occur regardless of whether or not you participate in this clinical research study. These risks are rare and may be outweighed by the potential benefits provided through the restoration of your vision. You should discuss with your study doctor the possible problems that may occur during or after this type of surgery and you should have all of your questions answered to your satisfaction.

Unforeseeable risks:

There may be risks or side effects related to the study drug/device that are unknown at this time. You will be notified of any significant new findings that become known that may affect your willingness to continue in the study.

Pregnant women, fertile females/males:

There may be unforeseen risks to an unborn child or nursing infant associated with your taking the study drug. Therefore, if you are capable of giving birth to or fathering a child, you and your sexual partner should use adequate birth control measures while you are in the study. These measures may include abstinence, oral contraceptives (birth control pills), IUD, diaphragm, approved hormone injections, condoms, or documentation of medical sterilization. If you are unwilling to do this, we ask that you not participate in this study.

Pregnancy tests will be performed on all women of child-bearing potential before beginning the study, at the screen visit. If you or your spouse becomes pregnant while taking part in this study you must notify the study doctor immediately. If birth control methods must continue after the study drug is discontinued, this time period should be provided to subjects.

KEEP OUT OF THE REACH OF CHILDREN
The drops given to you during the course of the study must be kept out of the reach of children or persons with limited ability to read and understand.

3. BENEFITS
Are There Benefits To Taking Part In The Study?
Participating in this study may benefit you by reducing the amount of eye complications after cataract surgery. This may result in a faster recovery of vision following surgery; however, this is not guaranteed. Additionally, your participation in a controlled clinical study helps to advance the understanding of how this type of medicine may prevent or reduce leakage at the back of the eye after cataract surgery.

4. ALTERNATIVES
What Other Options Are There?
You do not have to participate in this study to be treated for your condition. If you choose not to participate in this research study, your study doctor may use another anti-VEGF drug at the time of your surgery.

Rather than participate in this study, you may choose to be treated with alternative therapies. Please talk to your doctor about these and other options.

5. PRIVACY AND CONFIDENTIALITY
The medical and research information recorded about you for this research will be used within the Cleveland Clinic and/or disclosed outside the Cleveland Clinic. Tests and procedures done solely for this research study may be placed in your medical record to indicate your participation in this study. Except when required by law, your name, social security number, telephone number, address, or any other direct personal identifier will not identify you in your study records used outside of the study doctor's office. The information recorded about you as part of this research will be maintained in a confidential manner.

Upon completion of the study, you may have access to the research information if contained in the medical record. During the study, your access to research information about you will be limited. Preventing this access during the study keeps the knowledge of study results from affecting the reliability of the study. This information will be available should an emergency arise that would require your treating physician to know this information to assist in treating you.

In order to participate in this study, federal regulations require that you authorize the release of any health information that may reveal your identity. The persons and entities that you are authorizing to use or disclose your individually identifiable health information may include the study doctor, the study staff, Cleveland Clinic monitors/auditors and IRB, the study Sponsor **Regeneron/Bayer Pharmaceuticals, Inc.** and its agents, the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), other governmental agencies from foreign countries. Because of the need to release information to these parties absolute confidentiality cannot be guaranteed. The Cleveland Clinic also may use and disclose this information for treatment and payment reasons. The Cleveland Clinic must

comply with legal requirements that mandate disclosure in unusual situations. Once your personal health information is released it may be re-disclosed and no longer protected by federal privacy laws. The results of this research may be presented at meetings or in publications; however, your identity will not be disclosed in those presentation.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to **Rishi Singh, M.D. at The Cleveland Clinic i32, 9500 Euclid Avenue, Cleveland, Ohio 44195**. If you do so, your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of the research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. Even if you ask us to stop outside disclosures, information collected about you will be disclosed as required by state and federal law.

The Cleveland Clinic will not use or disclose the information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board gives permission after ensuring that appropriate privacy safeguards are in place. The Institutional Review Board is a committee whose job is to protect the safety and welfare of research subjects.
By signing this informed consent form, you are authorizing such access to your medical records. If you choose not to sign this consent form, you will not be permitted to participate in this research study.

6. RESEARCH RELATED INJURIES

What Happens If An Injury Occurs?

In the event you are injured as a result of participation in this research, medical care is available to you and will be billed to your insurance company. The cost of such medical care that is not covered by your medical insurance will be your responsibility. Every effort to prevent study-related injury will be taken by the study doctor and staff. In the event you are injured as a direct result of the study while following the study doctor's instructions and the study requirements, you should immediately contact your study doctor. Medical care will be made available to you to treat physical injury directly resulting from study procedures or medication. Your study doctor will make reasonable best efforts to seek reimbursement for the costs of such care and treatment from third party payers (Medicare/Medicaid, government or private insurance benefits) prior to submitting such costs to Sponsor, except where to do so would constitute fraud or other legal impropriety. There are no plans to provide compensation for lost wages, direct or indirect losses. You are not waiving any legal rights by signing this form. Further information about research related injury is available by contacting the Institutional Review Board at 216-444-2924.

7. COSTS

What Are The Costs?

The study drug or other study related tests/procedures/visits will be provided at no cost to you. The cost for routine tests and services that would normally be performed even if you don't participate in the study will be billed to you or your insurance provider.
There are no plans to provide financial compensation to you in the event the results from this research lead to the development of new products.

Parking will be paid for you at each visit. You will not receive any other compensation for participating in this study.

8. VOLUNTARY PARTICIPATION

What Are Your Rights As A Participant?

Taking part in this study is voluntary. You will be told of any new, relevant information from the research that may affect your health, welfare, or willingness to continue in this study. Your participation in the study may be ended at any time by the study doctor, the Sponsor, the U.S. Food and Drug Administration, or the Institutional Review Board with or without your consent. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to withdraw from the study you should discuss with your study doctor your decision to ensure a safe withdrawal.

9.QUESTIONS

Whom Do You Call With Questions Or Problems?

If you have any questions, concerns or complaints about the research, or develop a research-related problem, contact **Rishi Singh, M.D. at 216-445-9497 or 1-800-223-2273 extension 59497**. If you need assistance after hours or on weekends, call **1-800- 223-2273** and ask for the ophthalmology resident. You should contact the Institutional Review Board at (216) 444-2924 if you have questions about rights as a research subject.

10. SIGNATURE

Statement of Participant

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____	_____	_____
Participant Signature	Date	Time

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____ _____ _____
Signature of person obtaining consent Date Time