

**INFORMED CONSENT:** The *Standard* Care versus *C*orticosteroid for *RE*tinal Vein Occlusion (SCORE) Study

**TITLE OF PROJECT:** The *Standard* Care versus *C*orticosteroid for *RE*tinal Vein Occlusion (SCORE) Study: Two Randomized Trials to Compare the Efficacy and Safety of Intravitreal Injection(s) of Triamcinolone Acetonide with Standard Care to Treat Macular Edema: One for Central Retinal Vein Occlusion and One for Branch Retinal Vein Occlusion

### **PURPOSE OF THE STUDY**

#### **Request to participate:**

You are being asked to participate in this research study because you have macular edema (swelling in the center of the retina) from a blockage in a retinal vein (a retinal blood vessel): either a central retinal vein occlusion (CRVO) (a blockage in a larger retinal blood vessel) or branch retinal vein occlusion (BRVO) (a blockage in a smaller retinal blood vessel). The study is designed to find out if injection(s) of steroid into the eye are safe and effective in the treatment of macular edema compared to standard treatment.

Triamcinolone acetonide is a steroid approved by the United States Food and Drug Administration (FDA) for injection into joints and muscles for treatment of inflammatory conditions. Triamcinolone acetonide works by reducing inflammation (swelling). Triamcinolone acetonide has not been approved by the FDA for use in the eye, and is considered an investigational drug when used to treat macular edema (eye disease).

Several thousand patients have received injections into the eye of a preparation of triamcinolone acetonide called Kenalog. Kenalog is not made to use in the eye. Use of Kenalog has been associated with eye inflammation in some patients and it is believed that this may be because there are preservatives along with the triamcinolone acetonide in the Kenalog preparation. The preparation of triamcinolone acetonide being used in the study is specially made for injection into the eye and does not contain any preservatives.

Your participation in this study is voluntary. The study procedures and the possible risks, discomforts and benefits of participation are described below. Please read the information carefully and discuss any questions you have with your doctors before you decide whether or not to participate.

If you choose to participate in this study, you must sign this form, which includes your authorization for the use and disclosure of your health information that is collected as part of your participation in this study. If you do not provide permission for the use and disclosure of your health information, you will not be able to participate in this study.

#### **Background:**

The retina is a part of the eye that is similar to the film in a camera and produces images for the brain to understand. The macula is the part of the retina that you use to read or see fine detail. Retinal veins drain blood away from the retina back to your heart. A blockage in one of the large

retinal veins (central retinal vein occlusion - CRVO) or smaller retinal veins (branch retinal vein occlusion - BRVO) can result in fluid in the center of the retina (macular edema). This can result in decreased vision in that eye. Injecting a steroid directly into your eye may improve the vision in your eye, but also carries risks. This study is being done to compare the risks and benefits of this treatment.

If the vision loss is due to fluid in the retina associated with CRVO, laser treatment has not been shown to improve the vision. No other proven treatments are available to try to improve the vision. In some cases, vision may improve without treatment over many months to years. If you have a CRVO, standard care consists of observation of the fluid in the retina as well as monitoring the eye for the development of other complications such as increased eye pressure or the growth of abnormal blood vessels which may require treatment. For patients with CRVO, this study is designed to find out if injection(s) of steroid into the eye is safe and if this can lead to improved vision compared with patients with CRVO who receive standard care (observation).

If the vision loss is due to fluid in the retina associated with BRVO, laser treatment alone has been proven to help restore the vision in some patients. However, despite laser treatment, there are some patients who do not experience an improvement in vision and improved treatments for this condition need to be developed. If you have a BRVO, standard treatment consists of laser treatment to the retina if excessive blood is not present in the retina along with fluid in the retina (macular edema). If excessive blood is present in the retina, standard treatment consists of observation until enough blood has been reabsorbed so that laser treatment can be performed. For patients with BRVO, this study is designed to find out if injection(s) of steroid into the eye is safe and if this can lead to improved vision compared with patients with BRVO who receive standard care (observation or laser treatment to the retina, depending on how much blood is present in the retina).

**Purpose:**

The purpose of this study is to find out if injection(s) of triamcinolone acetonide into the eye are safe and effective in the treatment of macular edema in eyes with central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) compared to standard treatment.

**PROCEDURE**

Approximately 972 people will participate in this study at various medical centers in the United States. There will be at least 12 study visits over a period of up to 3 years if you are assigned to a group that is to receive injection(s). If you are assigned to a standard care group, there will be at least 10 study visits over a period of 3 years. If you are assigned to a group that is to receive injection(s) or if you receive laser treatment as part of the standard care group, you may require additional visits, depending on whether or not you require additional treatment.

If you agree to participate in this study, you will have some tests to see if you are eligible. You will be asked questions about your medical and medication history, and you will have your blood pressure measured. If you are a woman and can bear children you will be asked to give a urine sample to see if you are pregnant. See Section on Pregnancy and Contraception.

In addition, you will have a complete eye examination for both eyes, including:

- **Visual acuity:** You will be asked to read letters on a special eye chart.
- **Fluorescein angiography:** Fluorescein angiography is a test in which a dye is injected into a vein in your arm. The dye travels throughout the body, including the eyes. With a camera and flashes of light, a series of photographs of the retina is taken as the dye passes through it. The photographs will show where and what kinds of changes have occurred in the retina. The test takes about 20 minutes.
- **Optical coherence tomography (OCT):** This is a test that uses a light source to examine the retina and measure the thickness of the retina. You will be asked to sit in front of the machine and you will be asked by either a technician or photographer to look into a pattern of flashing and rotating red and green lights first with one eye then the other. The procedure takes approximately 5 minutes per eye to perform.
- **Eye examination:** An assessment of the cornea, lens, and retina, after dilating drops have been administered, will be performed. Also, the pressure in your eyes will be measured.

During some of the eye examinations, fundus photography will be performed. Fundus photography is a procedure in which bright lights will be shone into your eyes and pictures will be taken of the back of your eye (retina).

If your study doctor determines that you are eligible for the study, you will be randomly assigned (by chance, like the flip of a coin) to receive either injection(s) of triamcinolone acetonide or standard treatment. If you have CRVO, standard treatment is observation. If you have BRVO and an excessive amount of blood in the retina, standard treatment is observation. If you have BRVO and excessive blood is not present in the retina, standard treatment is laser treatment.

If both of your eyes meet the criteria for being part of the study, only one of your eyes will be randomly selected to receive either steroid injection(s) or standard treatment. The other eye cannot be entered into the study.

If you are randomized to receive an injection of steroid medication, you will receive one of 2 doses (4 mg or 1 mg). This study is designed such that you have a 1 in 3 (33%) chance of receiving a steroid injection with the 4 mg dose, a 1 in 3 (33%) chance of receiving a steroid medication with the 1 mg dose, and a 1 in 3 (33%) chance of receiving standard treatment. During the study period, you will be examined at least every 4 months and, depending on how your eye responds to treatment, you may be retreated as often as every 4 months. Thus, if you are randomized to receive steroid injection(s), you may receive an injection as often as every 4 months. Similarly, if you have a BRVO that does not have excessive blood present in the retina and are randomized to standard treatment, you may receive multiple laser treatments.

Before receiving the injection with triamcinolone acetonide, a local anesthetic (numbing medication) will be placed with a cotton tipped applicator into the lower part of your eye in the clear tissue that surrounds the white of your eye. Regardless of the diagnosis of your macular edema (CRVO or BRVO), if you are assigned to receive triamcinolone acetonide, after a few minutes, the study drug will be injected into your vitreous, which is the jelly-like substance inside your eye located between the back of your lens and your retina. If you are assigned to a standard treatment arm, no injection will be given. If you receive an injection, before leaving,

your doctor will give you an antibiotic eyedrop to place in your eye for 3 days following the injection.

For the laser treatment procedure, if you are assigned to a standard care group and your eye doctor determines that laser treatment to the retina may benefit you, 1 or 2 drops of a numbing agent are applied to the surface of the eye. A special contact lens is then placed on the eye during the laser beam application. You will be asked to remain still while the laser beam is applied. Minimal discomfort is anticipated during the laser beam treatment.

If you have BRVO and are assigned to a standard treatment arm, you will receive immediate laser treatment unless there is too much blood in the retina to permit laser treatment to be given. If your doctor is unable to perform laser treatment at the time you enroll in the study because there is too much blood in the retina, you will be observed and laser treatment will be given if the blood clears enough to permit application of laser treatment.

If you have CRVO, no laser treatment will be given for macular edema, regardless of your assignment to the treatment arms.

Follow-up visits will occur at least every 4 months. The need and timing of additional visits depends on your course of treatment. For example, if you receive an injection, you will also be examined within 1 week of each injection and 1 month following each injection. At each visit, your vision will be checked. Your eyes will be dilated for an eye examination and the pressure of your eye measured. Photographs of your retina will be taken, and OCT will be performed at certain study visits. Fluorescein angiography will be performed at Months 4, 12, and 24. In addition, at Months 12, 24, and 36 you will have your blood pressure measured.

## **RISKS**

Possible risks of the injection include the following:

- 1) We anticipate an approximately 100% chance of seeing floaters (things floating around inside your eye), which almost always resolve within a few days to weeks.
- 2) We anticipate a low chance [estimated at less than 1 in 100 (1%)] of retinal detachment (separation of the film-like layer of cells at the back of the eye) which may require surgery to treat. If a retinal detachment occurs and surgery is required, the surgery is usually successful. However, a retinal detachment can produce permanent loss of vision and even blindness.
- 3) We anticipate a low chance [estimated at less than 1 in 100 (1%)] of vitreous hemorrhage (bleeding in the gel inside the eye) which usually resolves within a few weeks. If it does not go away, surgery may be needed to remove the blood. This surgery is usually successful. However, a vitreous hemorrhage can produce permanent loss of vision and even blindness.
- 4) We anticipate a low chance [estimated at less than 1 in 100 (1%)] of endophthalmitis (infection of an entire eye) which would require treatment with antibiotic injections into the eye and possibly surgery. This treatment is usually successful. However, endophthalmitis can produce permanent loss of vision and even blindness.
- 5) Tiny droplets, about the size of the period on this page, have been observed in the vitreous cavity following injection of the SCORE Study steroid preparation. As of

October 5, 2006, this has been reported in 6 study participants out of 256 study participants (2.3%) who have received an intravitreal steroid injection in the study. These droplets have been reported before with intravitreal injection of various other medications. The source of the droplets is believed to be silicone oil that is used as a lubricant in the syringes and needles employed to deliver the medication. Silicone oil in large amounts is sometimes put into the vitreous during retinal detachment surgery. The amount of silicone oil in the eye after an intravitreal injection is a very tiny amount. We do not have any evidence that droplets of silicone oil are harmful to the eye. None of the participants in the study has reported any problems with their vision or any other problems due to the droplets. It is possible that the droplets could cause you to see floaters at certain times depending on the background in your field of view and the lighting.

Possible risks associated with triamcinolone acetonide include the following:

- 1) We anticipate that many patients will experience cataract (clouding of the lens of the eye) after treatment. We do not know how often a cataract develops from the steroid injection. However, we think there is a good chance that a cataract will develop. If a cataract develops, cataract surgery may be needed. In most cases, this surgery is effective in removing the cataract.
- 2) An increase in eye pressure could happen right after the injection or it could happen weeks to months later. If the eye pressure is high right after the injection, eye drops may be given to help lower the eye pressure. If the pressure is still high, fluid may be removed from the front part of the eye with a small needle. If the eye pressure goes up after several weeks to months, eye drops may be needed to lower the eye pressure. If the eye drops do not lower the eye pressure, it may be necessary to have surgery to lower the eye pressure. There is an approximately 3 in 10 (30%) chance of increased pressure in the eye which is usually reversible and can be treated with medications (e.g. eyedrops) but may require surgery. It is estimated that the chance of requiring surgery to lower eye pressure (called trabeculectomy surgery) is less than 1 in 20 (5%).

There may be additional conditions associated with the injection and triamcinolone acetonide that are not known at this time.

**Fluorescein angiography:** After the orange-colored dye is injected into your arm, your skin may turn yellow for several hours. The yellow color will disappear as your kidney removes the dye from your body. Because the dye passes through your kidneys, your urine will turn dark orange for up to 24 hours after the exam. Some participants may be slightly nauseous (upset stomach) during the exam, but their nausea usually lasts only a few seconds, and rarely, some may vomit. There is also a chance of fainting and a chance of bruising (black and blue mark) at the site of injection. If the dye leaks out of your vein during the injection, some of the skin around the injection site may feel like it is burning or become yellow. The burning sensation usually lasts only a few minutes, and the yellow color goes away in a few days. As with any drug, it is possible that you could experience an allergic reaction to the dye. Such allergic reactions include: itching, skin rash, an acute or sudden drop in blood pressure to shock levels with loss of consciousness and/or associated with seizures, including the possibility of death (the risk of death is about 1 in 250,000).

**Optical coherence tomography (OCT):** For the OCT, your pupils will be dilated. Your pupils will remain dilated for 4 to 6 hours. This may result in excess glare in brightly lit areas. Sunglasses will reduce this problem. You should not drive if your vision is impaired.

**Risks of eye examination and dilation:** Dilation of your pupils may cause some temporary glare and blurring of vision. Occasionally, there may be an allergic reaction to the medication. If this should occur, medication to control the allergic reaction will be administered. Rarely, dilation may cause the pressure in the eye to go up; if this should occur, you will be treated with eyedrops and, if necessary, laser surgery.

It is possible that complications and side effects of the study treatment that are unknown at this time may occur. You will be told of any new findings that develop which may affect your willingness to continue in the study.

### **PREGNANCY AND CONTRACEPTION**

**Pregnancy:** If you are a woman and can bear children, you will have a urine pregnancy test at the beginning of the study. If you are pregnant, you will not be allowed in the study. If you become pregnant during the study, you must inform the physician or the study coordinator that you are pregnant.

**Contraception:** The effect of the dye injected for the fluorescein angiography procedure on a fetus is unknown. If you are a woman who is sexually active and can bear children, you or your partner must use a reliable form of birth control from the time you enroll in the study until you are no longer in the study.

### **BENEFITS**

It is possible that you may not benefit from your participation in the study. No direct medical benefit to you can be assured from your participation in this study. As a result of your participation, your macular edema may improve; however, this cannot be guaranteed. If you are randomized to a standard treatment arm, no therapy with the study drug will be given and, therefore, you will not receive direct benefit from participation in this study. However, information obtained in this study may be of future benefit to both you and other patients with macular edema.

### **ALTERNATIVES**

The information obtained from this study will have no bearing on your medical treatment. You may choose to not participate in this study. For CRVO there are currently no proven treatments available. For BRVO you may choose to undergo laser treatment if your doctor determines you are eligible (for example, if there is not too much blood associated with the fluid in your retina) or to receive no treatment at all.

## **CONFIDENTIALITY& YOUR PROTECTED HEALTH INFORMATION**

*(Section Required by the HIPAA Privacy Rule – 45 CFR 164.508)*

By signing this form, you are giving permission for the use and disclosure of your health information that is collected as part of your participation in this study.

### **A. What health information about you may be used or disclosed?**

The results of your examinations and testing that are part of this study will be reported to the SCORE Data Coordinating Center in Rockville, Maryland along with information from all other participants in the study at this and all other participating clinics across the country. The photographs of your eyes, angiograms, and OCTs from your evaluations will be sent to the Fundus Photograph Reading Center for this study. The Fundus Photograph Reading Center is located at the Department of Ophthalmology & Visual Sciences at the University of Wisconsin – Madison in Madison, WI. This information will be identified to the SCORE Data Coordinating Center and the Fundus Photograph Reading Center only by a code number assigned to you. Federal privacy regulations provide safeguards for privacy, security, and authorized access. Except where required by law and as noted in the paragraph below, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of your eye doctor's office.

Results of the study will be reported in medical journals and may be presented at scientific meetings. However, at no time will any of the patients in the study be identified in any publication or at any meeting. Confidentiality of your records will be maintained and all records will be kept in accordance with current legal requirements. The research team will discuss the results of your tests with you during the study. You will be informed of the results of the study at the time they are made public.

### **B. Who may use or disclose and see or receive your health information?**

Reviewers of your health information may include representatives of the SCORE Data Coordinating Center (Rockville, MD), the Fundus Photograph Reading Center (Madison, WI) and Pharmaceutical Partner (Allergan, Inc., Irvine, CA) who are involved in the conduct of the study, the analysis of the data and the manufacturing of the study drug, any review board that oversees human investigations regulations for your doctor's office or institution, or any federal agency that oversees the conduct of clinical trials. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

### **C. Why do they need to see or receive your health information?**

As part of this study, the persons or entities listed above (see paragraph B) may see, receive, or use your health information to help conduct the study and/or to evaluate the results. Your records may also be reviewed in order to meet federal or state regulations.

### **D. Is there an expiration date?**

No. Your authorization for the use and disclosure of your health information will continue indefinitely.

**E. May you stop or cancel your permission for the use and disclosure of your health information?**

Yes. You may stop or cancel your permission for the use and disclosure of your health information at any time. You need only to contact your doctor or one of the medical staff at (telephone number) and provide a notice of cancellation to him/her in writing. However, when you stop or cancel your permission for the use and disclosure of your health information, you will no longer be part of the study.

When you stop or cancel your permission for the use and disclosure of your health information or when you withdraw from the study directly, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, your entire medical record may need to be reviewed. All data that have already been collected for study purposes up to the time of cancellation or withdrawal, and any new information about any adverse event related or potentially related to the study, will be sent to the SCORE Data Coordinating Center.

**F. Is your health information protected after it has been given to others?**

It is possible that your health information may be given out or disclosed again if the recipients named above (see paragraph B) are not required by law to protect the privacy of your health information. The SCORE Study DCC will make very effort to comply with the Privacy Regulations as required by law.

**FINANCIAL RESPONSIBILITY**

Any costs borne by you that may result from your participation in this study are your responsibility. The triamcinolone acetonide (study drug) will be provided at no cost to you. All other charges associated with your continuing medical care, including the injection procedure (if applicable), the traditional laser treatment (if applicable), photography and room charges, will be billed to you or your insurance provider in the normal fashion. If you develop a complication as a result of participation in this study (e.g. cataract or glaucoma) and require treatment for the complication (e.g. cataract surgery or surgery for glaucoma), the cost of the cataract surgery or surgery for glaucoma will be billed to you or your insurance provider in the normal fashion.

If you experience an unexpected adverse reaction as a direct result of the study drug being administered in this study, your reasonable expenses for medical treatment of such reaction will be reimbursed by the drug manufacturer, Allergan, to the extent that these expenses are not covered by medical, third party, or government insurance or programs.

In select cases, reimbursement for travel related expenses may be available as need warrants.

**COMPENSATION AND INJURY STATEMENT**

If injury occurs due to your involvement in this study, medical treatment will be available. You or your insurance company will be responsible for the costs of this medical care, unless you experience an unexpected problem that is a direct result of the new formulation of triamcinolone being administered in this study. If this should occur, your reasonable expenses for medical treatment of such reaction will be reimbursed by the drug manufacturer, Allergan, to the extent



that these expenses are not covered by medical, third party, or government insurance or programs. Compensation for lost wages and/or direct or indirect losses is not available.

### **VOLUNTARY PARTICIPATION AND WITHDRAWAL STATEMENT**

You may withdraw from the research study at any time. Your participation is completely voluntary. You may stop participating at any time, and you may refuse to answer any question if you don't wish to answer. Even if you do not want to join the study, or if you stop participating in it, you will still have the same quality of medical care available to you at the local site. The investigators reserve the right to remove you from the study without your consent at such time that they feel it is in your best interest medically or for administrative reasons.

### **OFFER TO ANSWER ANY QUESTIONS**

In case of a research-related injury, or if you have any questions, please contact Dr. X (Principal Investigator) at X (XXX) XXX-XXXX. You may ask questions in the future if you do not understand something that is being done. If you have any questions regarding your rights as a study subject, you may contact the Institutional Review Board administrator (Lesley S. Zajac at 1-813-975-8690). You will be given a signed copy of this form to keep. You will be informed of significant new findings that may alter your continued participation in this study.

**Subject's Name** (printed) \_\_\_\_\_

**Description of Representative's Authority to Act for the Study Subject**  
\_\_\_\_\_ (if applicable)

### **AGREEMENT TO HAVE THE TESTING DONE TO SEE IF I AM ELIGIBLE FOR THIS STUDY**

***By signing below, I agree to have this testing done. I authorize the use and disclosure of my health information collected as part of the eligibility testing.***

\_\_\_\_\_  
Signature of Subject or Authorized Representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

\_\_\_\_\_  
Date

APPROVAL DATE
<b>JUL 09 2007</b>
Jaeb Center for Health Research Institutional Review Board

AGREEMENT TO PARTICIPATE IN THIS STUDY

*I have read the explanation about this study. I have been given the opportunity to discuss the study and to ask questions. I hereby give my consent to take part in this study. I authorize the use and disclosure of my health information collected as part of my participation in this study.*

\_\_\_\_\_  
Signature of Subject or Authorized Representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

\_\_\_\_\_  
Date

I have personally explained the research to the subject or the subject's legally authorized representative and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

\_\_\_\_\_  
Signature of person obtaining informed consent

APPROVAL DATE

**JUL 09 2007**

Jaeb Center for Health Research  
Institutional Review Board