

INFORMED CONSENT TO BE IN A RESEARCH STUDY

SPONSOR:

NAME OF PROTOCOL: ST-601A-002a, A Phase 3 Multicenter, Randomized, Double-Masked, Placebo-Controlled Study of the Safety and Efficacy of Difluprednate in the Treatment of Inflammation Following Ocular Surgery

NAME OF PRINCIPAL INVESTIGATOR:

ADDRESS OF STUDY SITE(S):

PHONE: XXX-XXX-XXXX

Why is this research being done?

You are being asked to take part in a research study because you have inflammation in your eye one day after having surgery in that eye. The trauma to your eye after surgery sometimes causes inflammation in the eye. The purpose of this research study is to see how safe and effective difluprednate 0.05% eye drops are taken either 2 times or 4 times daily in people with eye inflammation after surgery. There will be approximately 216 people in this research study at about 10 different study sites, in the United States. Your participation in this study will last approximately 5 weeks and involve a total of 6 visits.

As part of this study, you could be given eye drops called difluprednate. Difluprednate has been shown to be effective for the treatment of post operative inflammation in the eye. Difluprednate is an investigational drug, which means it has not been approved by the U.S. Food and Drug Administration (FDA).

This study is sponsored by Sirion Therapeutics. The doctor in charge of the study is being paid by the sponsor to conduct this study.

This Informed Consent Form may contain words that you might not understand. Please ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about the research study. It will give you a description of the steps to be followed, any risks or discomforts you may experience, any benefits you may receive, and the general rules to be followed. You should take part in the study only if you want to. You may refuse to take part or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. Please read this Consent Form and ask as many questions as

needed. You should not sign this form if you have any questions that have not been answered to your satisfaction or if you do not wish to participate.

What will happen if you take part in this research study?

Before the study starts, you will be asked to sign this informed consent, give your medical history and to inform your doctor or his/her staff if you are taking any medications (over-the-counter, prescription, or vitamins). You must be honest and complete when providing your medical history. Giving false, incomplete, or misleading information about your medical history, including past and present medications, could seriously affect your health.

If you decide to participate in this research study, a number of tests and procedures will be performed to determine if you qualify to participate. Many of these tests are done during a normal eye exam. None are experimental. The tests and procedures include:

- Medical history
- Current medication history (up to 3 months prior)
- Visual acuity (how well you read the eye chart)
- Eye exam of the front of your eye and the back of your eye by using dilation drops to examine the back of your eye
- Eye pressure measurement (measure the pressure in your eye)
- Urine pregnancy test*
- Visual Analog Scale (grade your symptoms on a 100 mm scale with 0 = no symptoms and 100 = severe symptom; you place a line where you feel your symptoms are best represented on that line)
- Corneal cell density (a measurement of the number of cells on the surface of your cornea)

***Adult women who have started menstruating must have a negative urine pregnancy test. If you are minor and have started menstruating, the doctor will determine if you should have this test.**

If you qualify for the study, you will be randomly placed (assigned by chance, like the flip of a coin) into one of four treatment groups:

- Difluprednate 0.05%, 1 drop taken 2 times daily in the surgery eye
- Difluprednate 0.05%, 1 drop taken 4 times daily in the surgery eye
- Placebo, 1 drop taken 2 times daily in the surgery eye
- Placebo, 1 drop taken 4 times daily in the surgery eye

The placebo eye drops contain no active ingredients and are used in this study to see how well the difluprednate eye drop works.

Neither you nor the doctor will know which study treatment you are receiving. However, this information can be obtained if you have a problem or an emergency.

Study Visits and Procedures

If you qualify to be in this study, you will have to follow the study schedule. You will have to visit the clinic on Day 1, which is your first post-op visit, then at Day 3 or 4, Day 8, Day 15, Day 29, and 1 week following your last dose of study eye drops.

The following procedures will be performed at every study visit and will take about 45 minutes to complete:

- Update medical history
- Update current medication(s)
- Visual acuity
- Eye exam
- Visual Analog Scale
- Eye pressure measurement

In addition the following procedures will be performed at certain visits:

- Eye exam with dilating drops at Day 15 and one week following the last dose of study drops (an extra 20 minutes)
- Corneal cell density at one week following the last dose of study eye drops (an extra 15 minutes)

On the day 15 visit, the doctor will start to reduce your study eye drops as follows:

- If you were taking the eye drops 4 times a day, you will take the eye drops 2 times a day for one week, then once a day for one week, and then stop.
- If you were taking the eye drops 2 times a day, you will take the eye drops once a day for two weeks, and then stop.

What is experimental?

The following are being performed for the purposes of this study and are not considered standard care:

- use of study drug
- being randomized to a study treatment
- multiple study visits
- pregnancy tests

What are the risks of the study?

You should tell the person obtaining your informed consent about any other research studies you are currently involved in. Previous studies with patients have shown difluprednate to be well tolerated. During the study you will be watched carefully for any side effects.

The most common side effects reported with difluprednate have been an increase in the pressure in your eye and irritation or stinging when the drop is put in the eye.

During examinations of your eye, anesthetic drops are placed in your eye to numb it. This drop may sting when it is put in the eye.

Because this eye drop is investigational, all of its side effects may not be known. There may be other risks or discomforts that are not known at this time. You will be told of any information that is discovered during the course of this study that might affect your decision to continue being a part of the study.

What are the benefits to taking part in this study?

Your inflammation could get better, stay the same, or get worse. No direct benefit can be promised to you for your participation in this study, however, others may benefit from what is learned during this study.

What other options are there?

You do not have to participate in this study to get treatment for your post operative inflammation. Standard medical care for post operative inflammation in the eye is to take steroid eye drops. Talk to your doctor about your choices before you decide if you will take part in this study. Please ask the study doctor as many questions as you want. The answers could help you decide whether to be in this study.

Confidentiality and Your Protected Health Information

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

A. What health information can be used or disclosed?

The results of your exams and tests that are part of this study will be reported to Sirion Therapeutics in Tampa, Florida along with the information of the other participants in this study at this clinic and of all the other clinics that participate throughout the country. This information will be identified at Sirion Therapeutics only by a number code assigned to you. Federal Privacy Regulations provide safeguards for the privacy, security, and authorized access. Except when required by law, and as described in the next paragraph, you will not be identified by name, social security number, address, phone number, or any other personal identifier in the study records disclosed outside your eye doctor's office.

Study results can be reported in medical journals and could be presented at scientific meetings. However, at no time will any of the study patients be identified in any publication or at any meeting. All efforts will be made to maintain confidentiality of your records. All the records will be kept in accordance with the current legal requirements.

B. Who can use and disclose and see or receive your health information?

The people that review your health information could include representatives of

- Sirion Therapeutics or designated agencies and/or individuals
- Data Safety Monitoring Board
- The Food and Drug Administration (FDA)
- Investigators that are involved in the conduct of this study and the analysis of data
- The review board that protects research participants (also called “Institutional Review Board”)
- Any federal agency that supervises the conduct of clinical studies

If your study record is reviewed by any of these groups, they can also be provided with your medical record.

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

As part of this study, the people or groups mentioned before (see paragraph B) could see, receive, or use your health information to help conduct the study and/or evaluate the results. Your records could also be reviewed to comply with the federal and state regulations.

D. Is there an expiration date?

Your authorization for the use and the disclosure of your health information will continue until the end of the study, unless the state laws say otherwise. The end of the study is when the data analysis of the study is complete and the manuscripts are made public. After this time, the data will be de-identified which means that the connection can not be made between you and the data. This de-identified data could continue to be used and could be accessible to the general public.

E. Can you terminate or cancel your permission for the use and disclosure of your health information?

Yes. You may cancel your permission for the use and disclosure of your health information at any moment. You must provide a written cancellation to the study doctor. However, if you cancel your permission for the use and disclosure of your health information, you will no longer be allowed to participate in this study.

If you cancel your permission for the use and disclosure of your health information, or when you withdraw from the study, new data will no longer be collected unless the data has to do with adverse event. All the data that has been collected for the study up until the cancellation or withdrawal will still be reviewed. Any new information pertaining to an adverse event related to, or possibly related to, the study will still be reviewed.

F. Is your health information protected after it is given to others?

It is possible that your health information can be given or disclosed again if the recipients named above (see paragraph B) are not required by law to protect the privacy of your health information.

What if you are injured?

If injury occurs due to your involvement in this study, medical treatment will be available through your primary doctor, local emergency room, or the study doctor. You or your insurance company will be responsible for the costs of this medical care. No funds have been set aside for compensation for lost wages and/or direct or indirect losses.

Legal rights

You do not waive any of your legal rights by signing this form.

Who do you call with questions about the study or to report an injury?

The Principal Investigator (doctor) or his/her staff has explained this research study and has offered to answer any questions. If you need answers to any other questions about this research or to report a research related injury, call the Principal Investigator listed on this consent form.

XXXXXXXXXXXXXXXX, MD
Phone Number: (XXX) XXX-XXXX

If you have questions about your rights as a study participant, you should call the Institutional Review Board (IRB).

Alan Sugar, MD
New England Institutional Review Board
Phone Number: 1-800-232-9570

Do you have to participate in this study?

Your participation in this study is completely your choice. If you decide to participate, you can stop at any time. If you cancel your consent, you may be asked to return for a visit for safety reasons. You will get the same medical care whether or not you participate in this study. There will be no penalties if you choose not to participate or if you choose to stop your participation once you have started. You will be told about any significant information that is discovered that could affect your willingness to continue in the study.

The investigator or the sponsor, Sirion Therapeutics, New England Institutional Review Board or the FDA may stop your participation in the study without your permission at any time for the following reasons:

- If you do not follow the instructions of the doctor
- If it is discovered that you do not meet the study requirements
- If the study is canceled
- If the investigator decides that your continued participation in this study can be harmful to you

Will it cost anything to participate?

Study related exams, tests, procedures and study medication will be provided to you at no cost. You have the right to ask what it will cost for you to take part in this study.

You will be compensated \$XX per study visit up to a maximum of \$XXX, based upon time and procedures for each visit completed.

If you stop the study early you will be compensated for the visits you completed. The compensation may be used to offset the meal and travel expenses that you may incur during the course of the study.

VOLUNTEER'S STATEMENT:

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. I may contact Dr. XXXX if I have any more questions about taking part in this study. Dr. XXXX or the company he/she is employed by is being paid by the sponsor for my participation in this study.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study.

If I have any questions about my rights as a research subject in this study I may contact:

Alan M. Sugar, M.D., Chairman
New England Institutional Review Board
40 Washington Street, Suite 130
Wellesley, MA 02481
Telephone: 1-800-232-9570

By signing this form, I have not waived any of my legal rights.

I have read and understand the above information. I agree to participate in this study. I understand that I will be given a copy of this signed and dated form for my own records.

Study Participant (signature)

Date

Print Participant's Name

Person who explained this study (signature)

Date

Printed name of person who explained this study

Child's Assent

Study Title: A Phase 3 Multicenter, Randomized, Double-Masked, Placebo-Controlled Study of the Safety and Efficacy of Difluprednate in the Treatment of Inflammation Following Ocular Surgery

Principal Investigator: Dr. XXX

What is a research study?

When doctors and scientists want to learn more about a medicine, they have to test it on people to see if the medicine helps people and make sure it does not hurt them.

Why do you want me to be in this study?

The people who are running this study think that a medicine called difluprednate eye drops will help children like you who have swelling in the eye after having eye surgery. But, they have to be able to tell doctors how to use the medicine in children. That is why we are asking you to help us test difluprednate. You do not have to be in the study if you do not want to be.

What do I have to do?

If you choose to be in this study, Dr. _____ will :

- Ask about your health history
- Ask what medications you've taken
- Test how well you read the eye chart
- Examine the front of your eye and the back of your eye. The doctor will have to use special eye drops to examine the back of your eye
- Measure the pressure in your eye
- Urine pregnancy test*
- Ask you to grade your eye symptoms on a 100 millimeter scale with 0 = no symptoms and 100 = awful symptoms; you mark a line where you feel your symptoms are on that line
- Take a measurement of the number of cells on the surface of your cornea

***If you are a minor and have started getting periods, the doctor will determine if you should have this test.**

You will take either 2 or 4 eye drops a day for 2 weeks, and then the doctor will have you take the eye drops less times for another 2 weeks.

You will go to the doctor's office 6 times.

You can ask any question you want before you decide if you want to be in this research study or not. The doctor or nurse will answer your questions.

What if I do not want to be in this study?

You do not have to be in this study. If you do not want to be in the study, the doctor will not force you to be in it. If you decide to be in the study, but change your mind, you can stop being in the study.

If you do not want to be in the study, or if you change your mind, just tell the doctor or nurse. You might have to have some more tests to make sure you are OK, but then you will not be in the study any more.

Will I get anything for being in the study?

If you decide to be in this study, you will get paid \$XX every time you go to the doctor's office for a study visit.

Could I be hurt if I am in the study?

The medicine has been tried on many adults already, so the doctors really think that it will not harm you. But, it may not work as well in children. Also, the medicine might sting when it goes in your eye or can make the pressure in the back of your eye go up. The doctors will test the pressure in your eye at every visit.

For some of the tests, eye drops that numb your eye may have to be used. This drop might sting when it first goes in your eye.

If you feel sick or are afraid that something is wrong with you, tell an adult at once.

Now I think I know about the study and what it means - Here is what I decided:

- NO, I do not want to be in the study**
- OK, I will be in the study**

Your name (printing is OK)

Date

I certify that this study and the procedures involved have been explained to (Insert Subject's Name) in terms he/she could understand and that he/she freely assented to participate in this study.

Signature of Person Obtaining Consent

Date/Time