UNIVERSITY OF ROCHESTER MEDICAL CENTER

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SCHOOL OF MEDICINE AND DENTISTRY
SCHOOL OF NURSING
STRONG MEMORIAL HOSPITAL
UNIVERSITY MEDICAL FACULTY GROUP

DEPARTMENT OF DERMATOLOGY

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

Assessing the Impact of Pioglitazone on Squamous Cell Skin Cancer Incidence in High Risk Patients

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This consent form describes a research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully.

The study staff will explain this study to you. Please ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about and discuss with family or friends.

- Being in this study is voluntary – it is your choice.
- If you join this study, you can change your mind and stop at any time.
- If you choose not to take part, your routine medical care will not be changed in any way. There are risks from participating and you should understand what these mean to you.

Introduction

You are being asked to participate because you have had frequent squamous cell skin cancers (SCC) over the past year. Before you decide if you want to participate, you need to understand the purpose of the study, the possible risks and benefits, and what is expected of you. This process is called informed consent.

This consent form provides you with information on the risks and benefits of the study and seeks your authorization for the use and disclosure of the health information that will be obtained from you if you take part in this study. If you are fit to be in this study and decide to participate, it is important that you make every effort to complete all study

visits and procedures. However, your participation is voluntary and you have the right to stop your participation at any time.

This study is being conducted by Dr. Alice Pentland in collaboration with Dr. Sherrif Ibrahim of the University of Rochester's Department of Dermatology.

Purpose of Study

We are doing this study to find out if pioglitazone (also called Actos, a drug approved by the FDA to treat diabetes, but not for this indication) can decrease the number of new SCC cancers in people who have a high risk of developing skin cancer.

Specifically, the purposes of this study are to assess whether pioglitazone will:

- Decrease the number of new skin cancers you develop while taking the drug
- Decrease how aggressive the new skin cancers you develop are
- Change what proteins your skin cells make.

Description of Study Procedures

If you decide to take part in this study, and you qualify, your participation will be for 12 months. During that time there will be a total of 8 scheduled clinic visits. Subjects enrolling in this study must meet certain requirements. The study team will review all of the restrictions and requirements of the study with you to determine if you qualify for the study and to answer your questions.

This study is an open label study. "Open Label" means that both you and the study team will know you are receiving pioglitazone. The study drug will be a pill that you will take by mouth daily for 6 months. You will be assigned to one of two groups - you will either take Pioglitazone for the first 6 months of the study or for the second 6 months.

You will have your vital signs (blood pressure, temperature, breathing and heart rate) measured at each visit. You will also be asked about other medications you are taking and how you are feeling in general at every visit.

Because we are interested in knowing whether Pioglitazone treatment decreases the number of tumors that patients develop who have a high risk of developing squamous cell cancer of the skin, we will need to get a detailed medical history about the skin cancers you have developed in the previous year, as well as the medications and other illnesses you may have developed during that same time. By signing this consent to participate,

you are indicating that you are willing to have us obtain this information from your medical record.

Blood samples:
An important part of this study are the blood samples that will be taken during each of your visits. These blood samples have several different purposes:

1. Several samples will be taken to evaluate the safety of this drug. This will be done by looking to see if there are any changes in your blood compared to before you were given the study medication in order to see if there are any changes in your body, such as liver function, kidney function, blood sugar level etc.

2. Some samples are being taken to determine your eligibility.

All of the information that we collect from these samples helps us to better understand the way that your body deals with the study drug, and also any effect that the study medication might be having on your body.

WHAT WILL HAPPEN DURING THE STUDY

Visit 1: Screening Visit (Day -1, Week -3)

At or before the Screening visit you will be asked to read this informed consent form. No procedures relating to the study will be performed on you until you have provided consent. If, after you have read this consent form and all of your questions have been answered, you would like to participate in this study, you will be asked to sign this consent form. After you have signed this informed consent we will do some tests and procedures to see if you qualify to take part in this research study. The study team will review the results of these tests and procedures. If you do not qualify, the study doctor will tell you why.

At this visit, we will:

- Collect your demographic information (date of birth, gender, race, ethnicity)

- Ask about your medical history and Squamous Cell Cancer(SCC) personal and family history.

- Ask a number of questions about your current health status and about any medication you are taking or procedures you are undergoing.

- Give you a physical exam, including height, weight, and vital signs.
- The study doctor will assess your body for SCC.
- Blood samples will be taken, using a needle to collect blood from a vein in your arm. Approximately 3 tablespoons of blood will be drawn for routine tests to determine if you are eligible to participate in the study. The study doctor or study coordinator will explain to you this process and what will happen based on your test result. If you are a woman and able to get pregnant, this includes a pregnancy test.
- A urine sample will be obtained. If you are a woman and able to get pregnant, your urine will be tested to see if you are pregnant.
- You may be asked to not change the doses of your current medication(s) for SCC.
- If the study team determines that you are eligible to participate in the study and you agree to participate, you will be asked to return to the clinic in about 1 week to begin the study.

Visit 2: Baseline Visit/Day 1 (Week 0)

At this visit, if your study doctor determines you are eligible to participate in this study, you will be assigned to a group that takes Pioglitazone the first 6 months of the study or takes the drug during the second 6 months of the study. During the portion of the study where you are assigned to take Pioglitazone, you will be given a supply of pioglitazone 30 mg tablets to take daily.

At this visit, the following will happen:

- You will be asked some general questions about how you are feeling and about any medication you have taken or procedures you have had since your last visit.
- Your vital signs will be measured.
- A urine sample will be obtained. If you are a woman and able to get pregnant, a urine pregnancy test will be performed.
- The study doctor will perform a physical exam.

- The study doctor will assess regions of your body for the presence of areas suspicious for squamous cell skin cancer.

- If any suspicious areas are identified, Dr. Ibrahim will perform a skin biopsy. This biopsy will consist of removing the likely tumor containing area of skin from you. Before we take the biopsy, we will clean the area and give you an injection of a numbing medicine called lidocaine to reduce the pain. If needed after removing the piece of skin, we will put 1-2 suture(s) (or stitches) to help healing. This will take about 20 minutes. You will have a routine followup visit scheduled later to have the sutures removed, and any needed treatment for the cancer will be scheduled.
- If you are scheduled to take Pioglitazone, you will be given a supply we obtain for you from the Strong Study Pharmacy. Potential side effects that may occur will be reviewed. You will take ½ tablet for the first 2 weeks after starting the prescription to see if you tolerate the medication. Our office will contact you at the end of 2 weeks to see how you are doing. If you are tolerating pioglitazone treatment, you will increase your dose to one full tablet per day.

Visit 3: (Day 56, Week 8, ± 1 week)
Visit 4: (Day 112, Week 16, ± 1 week)
Visit 5: (Day 168, Week 24, ± 2 weeks)
Visit 6: (Day 224, Week 32 , ± 2 week)
Visit 7: (Day 280, Week 40, ± 2 weeks)

At these visits the following will occur:

- You will be asked some general questions about how you are feeling and about any medication you have taken or procedures you have had since your last visit.

- Your vital signs will be measured.

- A urine sample will be obtained. If you are a woman and able to get pregnant, a urine pregnancy test will be performed.

- The study doctor will perform a physical exam.

- You will bring your prescription bottle with you and the number of tablets remaining in your prescription will be counted.

- The study doctor will assess regions of your body for the presence of areas suspicious for squamous cell skin cancer.

- If any suspicious areas are identified, Dr. Ibrahim will perform a skin biopsy. This biopsy will consist of removing the likely tumor containing area of skin from you. Before we take the biopsy, we will clean the area and give you an injection of a numbing medicine called lidocaine to reduce the pain. If needed after removing the piece of skin, we will put 1-2 suture(s) (or stitches) to help healing. This will take about 20 minutes. You will have a routine followup visit scheduled later to have the sutures removed.

- You will be asked to have your blood drawn.

- If you are scheduled to take Pioglitazone, you will be given sufficient medication to last until your next visit. If your next visit is your final "on treatment" visit, you will be given enough pills so that you can continue to take the study drug until the date of the visit. The exact quantity of tablets may vary, since the final "on treatment" study visit may vary 7 to 14 days to accommodate your calendar. Potential side effects that may occur will be reviewed. You will take one tablet daily.

Visit 8: (Day 336, Week 40 +/- 2 weeks)

At this visit the following will occur:

- You will be asked some general questions about how you are feeling and about any medication you have taken or procedures you have had since your last visit.

- Your vital signs will be measured.

- A urine sample will be obtained. If you are a woman and able to get pregnant, a urine pregnancy test will be performed.

- The study doctor will perform a physical exam.

- The study doctor will assess regions of your body for the presence of areas suspicious for squamous cell skin cancer.

- If any suspicious areas are identified, Dr. Ibrahim will perform a skin biopsy. This biopsy will consist of removing the likely tumor containing area of skin from you. Before we take the biopsy, we will clean the area and give you an injection of a numbing medicine called lidocaine to reduce the pain. If needed after removing the piece of skin, we will put 1-2 suture(s) (or stitches) to help healing.

This will take about 20 minutes. You will have a routine followup visit scheduled later to have the sutures removed.

- You will be asked to have your blood drawn.

A total of about 1 cup of blood will be taken from you during the 36 weeks of this study. For comparison, when making a donation for transfusion, the standard blood donation is about two cups.

If you have a serious side effect from taking the study drug, additional blood may be taken.

Number of Subjects
Approximately 40 subjects will take part in this study.

Duration of the Study
Your participation in the study will last approximately 12 months. Each study visit will take approximately 2 hours. There will be 8 study visits altogether.

Risks of Participation
Allergic Reaction Risks Sometimes, people have serious allergic reactions to drugs. A severe allergic reaction could be life-threatening, and may result in death. Symptoms of allergic reactions include: rash, difficulty breathing, coughing, wheezing, sudden drop in blood pressure, swelling of the mouth, throat or eyes, seizures, flushing, a fast pulse, and sweating. If you believe you are having a serious allergic reaction, you should seek emergency medical treatment immediately, and alert the study doctor and study staff as soon as possible.

Heart Failure There is a risk that pioglitazone may cause or make heart failure worse in some patients. The signs that this may be happening are excessive rapid weight gain, shortness of breath or fluid retention (edema). You should report any problems with fluid accumulation to the study monitor.

Hepatic Effects : There have postmarketing reports of liver failure, sometimes fatal, and pioglitazone could not be excluded as the cause. Your liver will be monitored by blood work during the study, and if any changes are detected, pioglitazone treatment will be discontinued.

Vision Changes In postmarketing reports, macular edema has occurred, which can influence vision. Regular eye exams are recommended and any change in vision should be reported to the study monitor.

Fractures Patients with osteoporosis may have bone loss made worse, so patients taking pioglitazone should be sure their routine bone density assessments are up to date.

Pregnancy Premenopausal women may ovulate when taking pioglitazone who were not ovulating previously, increasing the risk of pregnancy. Appropriate contraception is needed.

Bladder Cancer Risk Use of pioglitazone is associated with a small increased risk of bladder cancer with longer duration of therapy (2 years) associated with larger risks.

There is also a risk of interaction with other medications you have been prescribed during your treatment. Taking Pioglitazone may change the way your body reacts to a new drug, so it is important to tell us at each visit if any of your medications have changed.

Be sure to tell the study doctor and/or study staff about any changes to your health during the study, including but not limited to any of the side effects described here.

Risks Associated with Blood Draws

Risks related to subcutaneous injection of the study drug and drawing blood may include discomfort, swelling, bruising, infection, bleeding, pain, lightheadedness, and/or redness at the site of the needle stick. If you feel faint, tell the study staff right away.

A description of this clinical trial will be available on http://www.ClinicalTrials.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 website at any time.

Benefits of Participation

You might not benefit from being in this research study. The potential benefit to you from being in this study might be a decrease in the number of squamous cell skin cancers you develop, or a decrease in their aggressiveness.

New Study Findings

If we discover anything that might make you change your mind about continuing in the study, we will let you know.

Alternatives to Participation
There are other treatments that may decrease the risk of squamous cell cancer...You should ask your study doctor about other medications to treat your risk of skin cancer.

Sponsor Support
The University of Rochester Department of Dermatology is sponsoring this study.

Costs
The University of Rochester's Department of Dermatology will pay for your pioglitazone prescription. However, some of the tests/procedures/exams (urinalysis, skin biopsy, blood tests) you will receive are standard care. You and/or your insurance company will be responsible for paying for any tests/procedures/exams that are done as part of your standard care. You are encouraged to discuss your coverage with your insurance provider.

Payments
You will not be paid for participating in this study.

Circumstances for Dismissal
You may be withdrawn from the study if you do not keep appointments for study visits or if you cannot complete study activities You may also be withdrawn from the study if your disease becomes worse or if your doctor feels that staying in the study is harmful to your health.

Compensation for Injury
If you are directly injured by the drug being studied, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. You will be reimbursed for reasonable and necessary medical costs for such care, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No other funds have been set aside to pay for such things as lost wages or expenses due to a current underlying illness or condition.

If your research injury is paid for by the University, we will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. This information will be used only in accordance with the law. If you are a Medicare beneficiary, information about the study you are in, and any payments made related to your injury, will be reported to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS requirements. This information will not be used for any other purpose.

Confidentiality of Records

The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will keep study records in a secure place and ensure that study personnel are aware of needed precautions to protect the security of your records. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor. If this does happen we will take precautions to protect the information you have provided. Results of the research may be presented at meetings or in publications, but your name will not be used.

Confidentiality of Records and Authorization to Use and Disclose

The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will keep study data on secure computers and train personnel in privacy protection. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigator for one.

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Past and present medical records related to the study
- Results of medical tests

Who may use and give out information about you?

- The study doctor and the study staff
- URMC and Affiliates

Your information may be given to:

- The Department of Health and Human Services
- The University of Rochester
- The U.S. Food and Drug Administration (FDA) may also need to inspect study records at some point during the study or even after it has been completed. In the event that this should occur, every effort will be made to keep identifying information about you private.
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Why will this information be used and/or given to others?

- To do the research

- To study the results
- To see if the research was done right

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this be permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
Yes. You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
No. There is a risk that your information will be given to others without your permission.

Contact Persons
For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact: **Dr. Sherrif Ibrahim at (585) 487-1440.**

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420315, Rochester, NY 14642, Telephone (585) 276-0005 or (877) 449-4441 for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;

- In the event the study staff could not be reached.

Voluntary Participation

Taking part in this study is voluntary. You are free not to take part or to withdraw at any time, for whatever reason. No matter what decision you make, there will be no penalty or loss of benefit to which you are entitled. In the event that you do withdraw from this study, the information you have already provided will be kept in a confidential manner.

SIGNATURE/DATES

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study.

Contact for Future Research:

The research we are doing now may lead to new questions. We may want to ask you to participate in future studies to help us answer those new questions. We would like your permission to contact you in the future for studies that are similar to this one.
Please initial on only one line:

_____ Yes, you may contact me in the future about other studies.
_____ No, I do not want you to contact me about other studies

Subject Consent

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

_____
Subject Name (Printed by Subject)

_____ _____
Signature of Subject Date

Person Obtaining Consent

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I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read the consent before signing.

_____
Name and Title (Print)

_____ _____
Signature of Person Obtaining Consent Date