INFORMED CONSENT FORM

Pre-Treatment of Highly Suspicious Pigmented Skin Lesions with Interleukin-2

QEII Hospital
Nova Scotia Health Authority
Halifax
Canada

Date: July 27th 2017
NCT Number: Not Yet Assigned

Prepared by:

Gordon Simms,
Room 5E2, 5th Floor
Sir Charles Tupper Medical Building
5850 College Street
Halifax, Nova Scotia
B3H 4R2, Canada
Informed Consent Form

STUDY TITLE: Pre-Treatment of Highly Suspicious Pigmented Skin Lesions with Interleukin-2

PRINCIPAL INVESTIGATOR: Dr. Carman Giacomantonio, Surgical Oncologist, 1276 South Park Street, Halifax NS, B3H 2Y9, Room 8-826 VG Bldg.

STUDY SPONSOR: Dr. Carman Giacomantonio

FUNDER: Paul Goldburg Foundation

1. Introduction

We would like to invite you to participate in a study, called “Pre-Treatment of Highly Suspicious Pigmented Skin Lesions with Interleukin-2”. We are approaching patients with pigmented lesions highly suspicious of melanoma to be part of this study. Before your lesion removal, we would like to treat your lesion with either IL-2 (Interleukin-2) or injectable saline (placebo) injection. IL-2 is now currently being used to treat patients with confirmed melanoma lesions. We are looking to find out if treating patients with highly suspicious lesions before lesion removal will prevent melanoma growth and spread.

Through a randomization process, you will receive either IL-2 treatment or an injectable saline (placebo) treatment. Before your first treatment, we will get a blood and urine sample from you. You will then get your treatment or placebo injection. One week later, you will receive your second treatment. You will have an incisional biopsy of your lesion one week after your second treatment and it will be sent to pathology for diagnosis. We will also collect another blood and urine sample at that time. It takes approximately four weeks to confirm results. If the results come back positive for melanoma, you will follow the normal standard of care treatment plan with your doctor.

Your response to the treatments for this study will be monitored at your visits. Your usual standard of care will be maintained and your treatment for potential positive melanoma results will not be delayed by becoming part of this study. You will simply receive an injection of either IL-2 or injectable saline (placebo) before your normal standard of care begins.

Being a part of this study is voluntary. Before you decide to be part of this study, you need to understand what the study is for, what risks you might take and what
benefits you might receive. This consent form explains how this study works. Your surgeon and/or the CDHA support staff will let you know the timeline for making your decision. It will depend on the date that your treatment starts.

Please ask your doctor or the CDHA support staff to clarify anything you do not understand or would like to know more about. Make sure all your questions are answered to your satisfaction before deciding whether to be a participant.

Your doctor and the CDHA support staff:

- Discuss the procedures with you
- Answer your questions
- Be available at any point before, during or after your treatment to deal with problems and answer questions

You are being asked to consider participating because you have a highly suspicious pigmented lesion that might be melanoma.

If you decide not to take part or if you leave and no longer wish to be a part of this study, your usual health care will not be affected.

2. Why is This Study Being Conducted?

Skin cancer is by far the world’s most common form of cancer – with more diagnoses annually than breast, prostate, lung, and colon cancers combined. Melanoma, the most aggressive form of skin cancer, has killed an estimated 1200 Canadians in 2016 alone.¹ When discovered early, melanoma can usually be cured with surgery alone, but once it metastasizes there are few treatment options.² Up until 2011, only two therapies were approved by the US food and drug administration (FDA) for the treatment of advanced metastatic melanoma (MM) – Dacarbazine (DTIC) and systemic Interleukin-2 (IL-2).³,⁴

IL-2 is a naturally occurring protein in the immune system, and has been used as a cancer immunotherapy for almost 40 years. Systemically administered (administered through blood) melanoma immunotherapies, such as IL-2, can be toxic to patients because it is administered at high doses.³ Intralesional administration (treatment administered directly into the lesion) of IL-2 is a simple method to deliver lower doses of IL-2 preventing toxicity experienced with higher doses.⁵

We aim to include 20-60 local participants over the next 24 months in a randomized, placebo-controlled, trial of intralesional IL-2 to assess the utility of treating highly suspicious lesions – to create a natural immune response and prevent spread of the disease. *We believe that a “Proactive” pre-treatment strategy with IL-2 is the future of melanoma therapy.*
3. How long will I be in this Study?

If you consent to being a part of this study, you will receive two treatments one week apart. You will be monitored for the duration of your treatment. If your lesions tests positive for melanoma, you will be monitored every 6 months for 5 years following your normal standard of care treatment. You will have blood drawn and a urine sample collected before your first and one week following your second treatment. You will have an incisional biopsy one week after your second treatment (as part of your normal standard of care). Blood, urine and lesion biopsy will occur at your scheduled appointment and therefore, no additional visits will be required.

4. How Many People Will Take Part In This Study?

We will invite 20-60 patients to participate over the next 2 years.

5. How is the Study Being Done?

Through a randomization process (by chance), you will receive either IL-2 treatment or an injectable saline (placebo) treatment. Neither you, the study staff nor the investigator(s) can influence which group you are in. You will have a 50% chance of being placed in either group. If you consent to be a part of this study, before beginning treatments we will collect some information such as, family history, medical history, and current medications.

Your doctor and CDHA support staff will organize your treatment plan with you. We will take a portion of blood and urine samples collected for our research study. We would also like to ask additional questions about your health, such as any new medications either prescribed, over the counter or naturopathic, and any other health conditions.

We plan to conduct analysis of your biopsied tissue, blood and urine samples. These analyses will look at how your immune system is affected in response to your treatment and what effect if any this has on your lesion. These studies will not require any of your time. We hope to have the initial analyses of your immune response completed within two years. We will be monitoring patient health over five years to determine if there was any overall benefit to the treatment.

If you decide you no longer wish to be part of this study, please contact your doctor or the CDHA support staff at any time. You will be asked to sign a form at that time. It will be your decision if you would also like to remove any stored tissue for research purposes. No further information will be collected for the study from that point onward. You will continue to receive normal standard of care for your diagnosis.
It is important that you tell your doctor about any drugs or medicines you are taking or wish to take. You must also tell us about anything unusual that is happening with your health. This includes any medical problems that seem to be getting worse. You should also tell your own doctor as quickly as possible, for your safety.

6. Are There Risks to the Study?

There are risks with this, or any study. To give you the most complete information available, we have listed many possible risks, which may appear alarming. We do not want to alarm you but we do want to make sure that if you decide to try the study, you have had a chance to think about the risks carefully. Please also be aware that there may be risks in participating in this study that we do not know about yet.

Minimal Risk: Patients receiving intralesional IL-2 treatment may develop mild flu-like symptoms, including fever, chills, malaise and diarrhea. These symptoms are brief and general resolve within 48 hours.

Minimal Risk: Treatment injections. There is a possibility of pain, bruising, swelling or itch related to the injection. These discomforts are minimal and brief.

Minimal Risk: Drawing Blood. There is a possibility of pain, bruising, swelling or infection related to giving blood. These discomforts are minimal and brief.

Minimal Risk: Breach of confidentiality. As with all research, there is a chance that confidentiality could be compromised; however, we are taking precautions to minimize this risk.

You may notice none, some, or all of these side effects and they may be mild or moderate. All side effects disappear after treatment is stopped. The principal investigator may prescribe medications to ease the discomfort you may experience if any of these side effects occur. If any severe reaction to the study drug occurs, the principal investigator may interrupt or discontinue the study drug treatment. The research team will be checking you closely to see if any of these side effects are occurring. There may be side effects that are not yet known. You must tell the research team about any new symptoms you experience.

The kind of information we will look for in the tissue analysis is not likely to tell you anything specific about your personal health. Even so, if someone allowed your genetic facts to become public knowledge, it could affect your ability to get or keep a job and/or your ability to get or keep various types of insurance, like life insurance. We think the chance of this ever happening to you is very small.

To protect your information, we will not keep your name or other information that may identify you with the sample; only a code number. Files that link your name to the code number will be kept in a secure place at the hospital. Although no one can absolutely
guarantee confidentiality, using a code number makes the chance much smaller that someone other than the research staff or other authorized groups or persons (discussed later in the consent form) will ever be able to link your name to your sample or to any test results.

Although your name will not be kept with the sample, information provided with your sample may have other facts about you such as your family history or medical history. These facts are important because they will help us learn whether or not the factors that cause metastatic melanoma to occur or get worse are the same or different in people with different family and medical histories. Thus, it is possible that research findings could one day help people of the same as you.

The study treatment is not known to react with commonly prescribed medications, however, you should ask the research team if the study treatment could interfere with your medications before consenting to be in this study. You should also consult with the research team before taking any new medications.

You will be told about any new information that might reasonably affect your willingness to continue to participate in this study as soon as the information becomes available to the research team.

7. Are There Benefits of Participating in this Study?

We cannot guarantee or promise that you will receive any benefits from this research. There is a chance the research and knowledge gained may help you in the future if there is a recurrence, however there is a greater probability that research will help future patients with highly suspicious pigmented lesions and future melanoma patients, if new therapies and preventative treatments are developed and/or perfected.

8. What Happens at the End of the Study?

It is anticipated that the tissue, blood and urine analysis results will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

9. What Are My Responsibilities?

As a study participant you will be expected to:

- Follow the directions of the CDHA support staff;
- Report all medications being taken or that you plan on taking;
- Report any changes in your health to the CDHA support staff;
• Report any problems that you experience that you think might be related to participating in the study;
• Have blood and urine samples collected at appointments.

10. Can My Participation in this Study End Early?

Yes. If you chose to participate and later change your mind, you can say no and stop the research at any time. If you wish to withdraw your consent, please inform your doctor. If you choose to withdraw from this study, your decision will have no effect on your current or future medical treatment and healthcare. Any unused tissue, blood and urine samples will be discarded, but any data collected from testing your sample up until that point will remain part of the research.

Also, the Nova Scotia Health Authority Research Ethics Board and the principal investigator have the right to stop patient recruitment or cancel the study at any time.

If you are withdrawn from this study, the CDHA support staff will discuss the reasons with you and plans will be made for your continued care outside of the study.

If you withdraw your consent, the information about you and donated tissue that was collected before you left the study will still be used. No new information about you will be collected (and no further testing of your donated tissue, blood or urine will be done) without your permission.

11. What Will Happen to My Sample After the Study is Over?

If you agree to have your sample stored for future research, we will store the sample under a code number and we will keep the file that links the code number to your name private. We may share the samples with other researchers, but we will not give other researchers any information that would allow them to identify you. We will always know which sample belongs to you, but other researchers will not. We will not send your samples to other countries.

12. What About New Information?

You will be told about any other new information that might affect your health, welfare, or willingness to stay in the study and will be asked whether you wish to continue taking part in the study or not.
13. Will It Cost Me Anything?

There will be one extra visit and there may be associated travel costs. There will be no other costs associated with the study.

Research Related Injury

If you become ill or injured as a direct result of participating in this study, necessary medical treatment will be available at no additional cost to you. Your signature on this form only indicates that you have understood to your satisfaction the information regarding your participation in the study and agree to participate in the study. In no way does this waive your legal rights nor release the principal investigator, the research team, the study sponsor or involved institutions from their legal and professional responsibilities.

14. What About My Privacy and Confidentiality?

Protecting your privacy is an important part of this study. Every effort to protect your privacy will be made. If the results of the tissue analysis are presented to the public, nobody will be able to tell that you were in the study.

However, complete privacy cannot be guaranteed. For example, the principal investigator may be required by law to allow access to research records.

If you decide to donate tissue, blood and urine, the research team will look at your personal health information and collect only the information they need for this study. “Personal health information” is health information about you that could identify you because it includes information such as your:

- Name;
- Address;
- Telephone number;
- Age or month/year of birth (MM/YY);
- Information from the study interviews and questionnaires;
- New and existing medical records; or
- The types, dates and results of various tests and procedures.

If you decide to be a part of this study, once we take your tissue, blood and urine samples, we will assign it a code number. We will separate your name and any other information that points to you from your sample. We will keep files that link your name to the code number in a secure place away from your sample.
Access to Records

Other people may need to look at your personal health information to check that the information collected for the study is correct and to make sure the study followed the required laws and guidelines. These people might include:

- The Nova Scotia Health Authority Research Ethics Board (NSHA REB) and people working for or with the NSHA REB because they oversee the ethical conduct of research studies within the Nova Scotia Health Authority.

Use of Your Tissue, Blood and Urine Analysis Information

Any tissue, blood or urine analysis data about you that is sent outside of the Nova Scotia Health Authority will have a code and will not contain your name or address, or any information that directly identifies you.

De-identified study data may be transferred to:

- Regulatory authorities within Canada.

  Tissue, blood and urine analysis data that is sent outside of the Nova Scotia Health Authority will be used for the research purposes explained in this consent form.

  The research team will keep the information they see or receive about you confidential, to the extent permitted by applicable laws. Even though the risk of identifying you from the study data is very small, it can never be completely eliminated.

  The research team will keep any personal health information about you in a secure and confidential location indefinitely. Your personal health information will not be shared with others without your permission.

  We may continue to review your health records for safety and data accuracy indefinitely or until you withdraw your consent.

  You have the right to be informed of the results of this tissue analysis once the entire study is complete.

  The Research Ethics Board and people working for or with the Research Ethics Board may also contact you personally for quality assurance purposes.

Your access to records

You have the right to access, review, and request changes to your study data.
15. Declaration of Financial Interest

Dr. Carman Giacomantonio is receiving reimbursement to conduct tissue, blood and urine analyses. The amount of payment is sufficient only to cover the costs of conducting the study, and this work is not being done for profit.

16. What About Questions or Problems?

For further information about this study you may call your surgeon and principal investigator, who is the person in charge of this study.

The principal investigator Dr. Carman Giacomantonio.
Telephone: 902-473-6177.

The CDHA support staff Dr. Gordon Simms.
Telephone: 902-489-0168.

17. What are My Rights?

You have the right to all information that could help you make a decision about participating in this study. You also have the right to ask questions about this study and your rights as a research participant, and to have them answered to your satisfaction before you make any decision. You also have the right to ask questions and to receive answers throughout this study.

If you have any questions about your rights as a research participant, contact Patient Relations at (902) 473-2133 or healthcareexperience@nshealth.ca

In the next part you will be asked if you agree (consent) to join this study. If the answer is “yes”, please sign the form.
18. Consent Form Signature Page

I have reviewed all the information in this consent form related to the study called:

“Pre-Treatment of IL-2 for Highly Suspicious Pigmented Skin Lesions”

I have been given the opportunity to discuss this study. All my questions have been answered to my satisfaction.

I authorize access to my personal health information, and research study data as explained in this form.

This signature on this consent form means that I agree to take part in this study. I understand that I am free to withdraw at any time without affecting my future care.

______________________________        _______________________
Signature of Participant        Name (Printed)
___________________________________________________________
Year Month Day*

______________________________        _______________________
Signature of Person Conducting Consent Discussion        Name (Printed)
___________________________________________________________
Year Month Day*

______________________________        _______________________
Signature of Investigator        Name (Printed)
___________________________________________________________
Year Month Day*

______________________________        _______________________
Signature of Participant’s Substitute Decision Maker        Name (Printed)
___________________________________________________________
Year Month Day*

______________________________        _______________________
Signature of Impartial Witness        Name (Printed)
___________________________________________________________
Year Month Day*

If the consent discussion has been conducted in a language other than English, please indicate: _______________
Language

______________________________        _______________________
Signature of Translator        Name (Printed)
___________________________________________________________
Year Month Day*

*Note: Please fill in the dates personally

I will be given a signed copy of this consent form.
Another way to find out what will happen during this study is to read the study plan below. Start reading at the top and read down the list, following the arrows.

1. Informed Consent
2. Randomization
3. Patient blood, urine and personal health information collected
4. First treatment of Injectable Saline (Placebo)
5. Second treatment of injectable saline (placebo)
6. Biopsy performed and blood and urine collection. Tissue sent for standard pathology assessment
7. Standard of care follow up for patients with lesions that test positive for melanoma
8. First treatment of study drug IL-2
9. Second treatment of study drug IL-2
Schedule of Assessments

Boxes marked with an X show what will happen at each visit.

<table>
<thead>
<tr>
<th></th>
<th>Visit 1 Week 1</th>
<th>Visit 2 Week 2</th>
<th>Visit 3 Week 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>1.5 hour</td>
<td>0.5 hour</td>
<td>1 hour</td>
</tr>
<tr>
<td>Informed consent</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Blood test</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Urine test</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Treatment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Il-2 or placebo</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Lesion Removal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References