Informed Consent Form for Participation in a Research Study

Expression of Biomarkers in Gastric Cancer and the Effect of Neoadjuvant Chemotherapy

Protocol ID: RES0037162

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Sponsor/Funder(s): Edmonton Civic Employees Fund

Non-Emergency contact numbers are noted at the end of this document under the section heading “WHO DO I CONTACT FOR QUESTIONS?”.

For assistance with terminology within this consent form, please refer to the Canadian Cancer Society Glossary of Terms at http://info.cancer.ca/e/glossary/glossary.html.

You are being invited to participate in a research study because you have been diagnosed with cancer of the stomach or Gastric cancer. This consent form provides detailed information about the study to assist you with making an informed decision. Please read this document carefully and ask any questions you may have. All questions should be answered to your satisfaction before you decide whether to participate.

The study staff will tell you about timelines for making your decision. You may find it helpful to discuss the study with family and friends so that you can make the best possible decision within the given timelines.

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health-related benefits to which you are entitled.

The study doctor, who is one of the researchers, or a research nurse will discuss this study with you and will answer any questions you may have. If you do consent to participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Gastric cancer is an important cause of deaths from cancer worldwide. While it is not as common in Canada, each year about 255 people in Alberta are diagnosed with Gastric Cancer. The only possible cure for gastric cancer involves surgery and sometimes chemotherapy and radiation therapy. Despite aggressive treatment, many patients diagnosed with this disease

cannot be cured. We are seeking to better understand this cancer to see if we can develop better, more effective treatments in the future.

The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to help us understand if there are certain markers (called biomarkers) that are turned on (upregulated) or turned off (downregulated) in gastric cancer tissue. If we can identify certain markers that are turned on or off then we can better understand the pathways that are used by the cancer to grow. Once we understand these pathways then we can hopefully predict response to treatments better and even develop new treatments for this cancer.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?

You do not have to take part in this study, in order to receive continued medical care.

Please talk to the study doctor or your care doctor about the known benefits and risks of these other options before you decide to take part in this study. Your study or care doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 125 people will take part in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

STUDY INTERVENTION

If you agree to take part in this study, you will have 6-8 small pieces each (biopsies) of your cancer and normal stomach tissue collected for study purposes at the time of your endoscopy. The tissues will be used to detect molecules (biomarkers) that could potentially be used as new targets of treatment for gastric cancer. If you undergo chemotherapy before surgery, then at the time of your surgery you will have biopsies taken again at the time of operation to see if the tissue and the biomarkers changed as a response to the chemotherapy. These small pieces of tissue will be analyzed to see if there are biomarkers in your cancer that are upregulated or downregulated. We would look at the indicators in the final pathology report such as tumor size, tumor grade, evidence of perineural invasion, lymphovascular invasion to see if the biomarkers predict for any of these indicators. For example high grade, lympovascular invasion and perineural invasion are all bad prognostic signs. If some of the biomarkers were associated with high incidence of these indicators, this would be useful to know because we can predict who should get chemotherapy.

STUDY PROCEDURES

Tissue Collection (Mandatory)

As part of standard care, you will need to have a tissue biopsy. A tissue biopsy is a type of surgical procedure, which will remove a small pea sized pieces of your gastric cancer. This will be done during one of your planned endoscopy procedures and you will either be sedated or under a general anesthetic at the time. This procedure has a very small risk of bleeding associated with it.

In addition to standard blood work we will collect a small amount (40-50 ml) of blood to analyze the presence of cancer cells in your blood and your immune system. Puncture sites will be monitored for bleeding/hematoma and pressure will be applied until cessation of bleeding when necessary. If anemic to the point of being symptomatic or requiring blood transfusion no blood will be taken.

These tissue samples will be sent to a laboratory at the Li Ka Shing Centre, University of Alberta where they will be processed to evaluate the expression of biomarkers and their response to anti-cancer drugs.

Identification of Samples

To protect your identity, the information that will be on your samples will be limited to your health care number and date of birth. Before transfer to the laboratory the health care number and date of birth will be removed and the sample will be assigned a number.

Despite protections being in place, there is a risk of unintentional release of information that could lead to loss of privacy. Due to technological advances in genetics, there is also a risk of unintentional release of genetic information from the samples. This information can be linked back to you and can lead to possible future discrimination in employment or insurance, against you or your biological relatives.

Withdrawal of Samples

If you no longer want your samples to be used in this research, you should tell the study doctor. The study doctor will ensure the samples are returned to the hospital from which they were obtained, if needed, or destroyed.

If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

WHAT ARE THE POTENTIAL SIDE EFFECTS FROM PARTICIPATING IN THIS STUDY?

Risks and side effects related to a biopsy at the time of endoscopy are very rare. There is a small chance of bleeding or perforation.

Side effects of a blood sample include pain at the site of puncture. The risk for infection is low

and the risk of anemia due to repeated blood draws is low.
The risks and side-effects of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

Participation in this study may or may not be of personal benefit to you.

However, based on the results of this study, it is hoped that in the long-term, patient care for people diagnosed with gastric cancer can be improved.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions
- Attend all scheduled study visits and undergo all of the procedures described above

HOW LONG WILL I BE PARTICIPATING IN THIS STUDY?

The researchers will be collecting data on your health for 5 years after you enter into the study. Apart from the extra biopsies that will be taken, there will be nothing else added above your regular care which typically involves follow-up from the time of diagnosis for at least 5 years. Follow up will involve annual or semi-annual follow up visits with your doctor to see how you are doing. Blood tests and imaging tests such as CT SCANS may be ordered as well depending on how you are doing.

WILL THERE BE ANY LONG-TERM FOLLOW-UP INVOLVED WITH THIS STUDY?

All patients with gastric cancer are typically followed up for at least 5 years and this would not change whether you participate in this study or not.

The study team may attempt to obtain study-related information about your health from you or from other private sources, including your care physician. This may include contacting you again by phone or letter, but only if you have not withdrawn your consent for future contact. However, contacting you, your care physician or using other private sources of information, is optional, please indicate your decision using the check boxes below.

You give permission to the study doctor or member of the study team to attempt to obtain study-related information about your health status. This may include contacting your care physician, or by contacting you by phone or letter (i.e., future contact).

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of care physician: _____

In addition, the study team may also attempt to obtain study-relevant information about your health information from public sources such as national patient registries (e.g., cancer registries)

If the study doctor needs to follow up with you but cannot locate you, either because you have moved and not updated your contact information or if, for some reason, your contact information is no longer accurate, the study doctor would like to obtain your new contact information (e.g., address, telephone number) by calling or writing to the persons you've named as your secondary contacts. This is optional, please indicate your decision using the check boxes below.

You give permission to the study doctor or member of the study team to contact your secondary contacts if the study doctor or study team no longer have accurate contact information for you.

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of secondary contacts: _____

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

You can choose to end your participation in this research (called early withdrawal) at any time without having to provide a reason. If you choose to withdraw early from the study without finishing the intervention, procedure or follow-up, you are encouraged to contact the study doctor or study staff.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study.

If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study doctor know if you choose this.

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the study doctor and study staff will only collect the information they need for this study.

Records identifying you, including information collected from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your identifiable medical/clinical study records at the site where these records are held for quality assurance purposes and/or to verify that the information collected for the study is correct and follows proper laws and guidelines:

- The Health Research Ethics Board of Alberta – Cancer Committee, which oversees the ethical conduct of this study;

Any disclosure of your identifiable health information will be done in accordance with federal and provincial laws including the Alberta Health Information Act (HIA). The organizations listed above are required to have organizational policies and procedures to protect the information they see or receive about you, except where disclosure may be required by law. The study doctor will ensure that any personal health information collected for this study is kept in a secure and confidential location as also required by law.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be analyzed and disseminated in the scientific community interested in the study of gastric cancer.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. Every effort will be made to keep your identifiable information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

A copy of the consent form that you sign to enter the study will be included in your health record/hospital chart.

WILL MY HEALTHCARE PROVIDER(S) BE INFORMED OF MY PARTICIPATION IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like. If you are undecided, the study doctor can discuss this with you.

WILL THERE BE ANY COSTS INVOLVED WITH PARTICIPATING IN THIS STUDY?

Participation in this study will not involve any additional costs to you or your private health care insurance.

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

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

you would like to be informed of these results, please contact the study doctor.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?

There are no conflicts of interest declared between the study doctor and sponsor of this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME AS A RESEARCH PARTICIPANT?

If any clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity at that time to decide whether you wish to be made aware of that information.

WHO DO I CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to the study doctor, co-investigator or study nurse. These person(s) are:

Dr. Dan Schiller	780-413-7766
Name	Telephone
Rose Cornand	780-413-7766
Name	Telephone
Dr. Gina Rayat	780-492-6894
Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee at:

Telephone: 780-423-5727 Toll Free: 1-877-423-5727

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	No
Do you understand that you have been asked to take part in a research study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand the potential benefits of taking part in this study?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐
Do you understand that you are free to leave the study at any time, without having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information and specimens if applicable?	☐	☐
Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

By signing this form I agree to participate in this study.

Part 2 - to be completed by the study doctor or designee who conducted the informed consent discussion. Only complete this section if the potential participant has **agreed** to participate.

I believe that the person signing this form understands what is involved in the study and has freely decided to participate.

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

Part 3 - to be completed only if the participant is unable to read or requires assistance of an oral translator/interpreter.

- The informed consent form was accurately explained to, and apparently understood by the participant.

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

You will be given a copy of this signed and dated consent form prior to participating in this study.

Supplementary Material

Comparison of IHC biomarkers with clinicopathologic factors

Stage (n = 43)

Variable	Stage I, N = 11[1]	Stage II, N = 10[1]	Stage III, N = 8[1]	Stage IV, N = 14[1]	p-value[2]
CD4/CD8 Ratio	1.8 (1.3, 3.0)	2.4 (1.6, 2.8)	1.5 (1.0, 2.4)	1.4 (1.0, 2.8)	0.8
Unknown	0	0	0	1	
CD4	14 (11, 31)	16 (12, 21)	6 (4, 11)	15 (8, 23)	0.11
CD8	8 (4, 19)	7 (4, 11)	7 (3, 9)	8 (5, 12)	0.7
Unknown	0	0	0	1	
Galectin-3	43 (30, 53)	47 (35, 53)	45 (25, 55)	46 (33, 68)	0.9
E-cadherin	19 (10, 28)	16 (8, 30)	24 (21, 27)	7 (1, 21)	0.2
E-cadherin H-score	22 (13, 38)	21 (9, 46)	28 (26, 38)	8 (1, 32)	0.15

[1]Median (IQR)

[2]Kruskal-Wallis rank sum test

Lymphovascular Invasion (n = 35)

Variable	Negative, N = 19[1]	Positive, N = 16[1]	p-value[2]
CD4/CD8 Ratio	2.24 (1.46, 2.93)	1.34 (0.87, 2.56)	0.12
CD4	13 (10, 24)	14 (6, 23)	0.5
CD8	8 (3, 11)	8 (6, 11)	0.9
Galectin-3	43 (29, 53)	45 (37, 55)	0.7
E-cadherin	20 (13, 28)	8 (5, 25)	0.2
E-cadherin score	H-27 (14, 41)	11 (5, 30)	0.2

[1]Median (IQR)

[2]Wilcoxon rank sum exact test

Carcinomatosis (n = 38)

Variable	Negative, N = 29[1]	Positive, N = 9[1]	p-value[2]
CD4/CD8 Ratio	1.7 (1.2, 2.8)	1.7 (1.1, 4.9)	>0.9
Unknown	0	1	
CD4	12 (6, 24)	16 (10, 18)	0.9
CD8	8 (4, 11)	8 (4, 14)	0.8
Unknown	0	1	
Galectin-3	43 (30, 55)	47 (44, 70)	0.5
E-cadherin	20 (7, 27)	9 (2, 25)	0.4
E-cadherin score	H-25 (7, 38)	15 (3, 37)	0.4

[1]Median (IQR)

[2]Wilcoxon rank sum exact test

Perineural Invasion (n = 33)

Variable	Negative, N = 20[1]	Positive, N = 11[1]	p-value[2]
CD4/CD8 Ratio	2.49 (1.61, 3.09)	1.07 (0.76, 2.37)	0.054
CD4	15 (11, 24)	7 (5, 24)	0.2
CD8	8 (3, 10)	8 (5, 11)	0.9
Galectin-3	43 (30, 49)	53 (44, 63)	0.066
E-cadherin	20 (6, 30)	18 (6, 24)	0.6
E-cadherin H-score	25 (7, 44)	23 (7, 28)	0.7

[1]Median (IQR)

Tumour Grade (n = 43)

Variable	G1, N = 1[1]	G2, N = 10[1]	G3, N = 31[1]	Gx, N = 1[1]	p-value[2]
CD4/CD8 Ratio	1.4 (1.4, 1.4)	2.1 (1.6, 2.8)	1.9 (1.1, 3.0)	1.6 (1.6, 1.6)	0.9
Unknown	0	0	1	0	
CD4	6 (6, 6)	13 (8, 22)	14 (7, 24)	14 (14, 14)	0.7
CD8	4 (4, 4)	7 (3, 10)	8 (5, 12)	8 (8, 8)	0.7
Unknown	0	0	1	0	
Galectin-3	17 (17, 17)	39 (29, 47)	47 (34, 63)	69 (69, 69)	0.2
E-cadherin	26 (26, 26)	19 (7, 30)	16 (7, 28)	3 (3, 3)	0.5
E-cadherin H-score	32 (32, 32)	23 (8, 42)	22 (7, 40)	3 (3, 3)	0.5

[1]Median (IQR)

Lauren Classification (n = 41)

Variable	Diffuse, N = 26[1]	Intestinal, N = 13[1]	Mixed, N = 2[1]	p-value[2]
CD4/CD8 Ratio	2.1 (1.2, 2.8)	1.6 (1.2, 2.5)	2.6 (2.2, 3.0)	0.7
Unknown	1	0	0	
CD4	13 (8, 21)	15 (7, 24)	16 (11, 21)	>0.9
CD8	8 (5, 11)	8 (4, 14)	5 (4, 7)	0.7
Unknown	1	0	0	

[1]Median (IQR); [2]Kruskal-Wallis rank sum test, Fisher's exact test

Galectin-3	47 (32, 67)	37 (29, 48)	37 (34, 41)	0.4
E-cadherin	11 (6, 25)	25 (13, 31)	3 (2, 4)	0.043
E-cadherin H-score	17 (7, 35)	29 (15, 44)	3 (2, 5)	0.057

[1]Median (IQR)

[2]Kruskal-Wallis rank sum test

Tumour Location (n = 43)

Variable	Distal, N = 14[1]	Proximal, N = 26[1]	Whole stomach, N = 3[1]	p-value[2]
CD4/CD8 Ratio	2.0 (1.3, 3.1)	1.4 (1.0, 2.8)	2.8 (2.5, 10.3)	0.2
Unknown	0	1	0	
CD4	21 (11, 24)	12 (6, 21)	16 (12, 17)	0.4
CD8	8 (4, 14)	8 (5, 11)	6 (3, 7)	0.6
Unknown	0	1	0	
Galectin-3	45 (38, 53)	46 (30, 61)	20 (20, 45)	0.7
E-cadherin	18 (7, 29)	16 (6, 27)	26 (17, 34)	0.6
E-cadherin H-score	22 (8, 41)	20 (7, 37)	46 (28, 54)	0.5

[1]Median (IQR)

[2]Kruskal-Wallis rank sum test