Consent for participating in a clinical study

Treating liver metastases using electrochemotherapy

What do I need to know about the clinical study?

You are invited to participate in a clinical study (hereinafter: 'the study') in which the research team will evaluate the efficacy and potential toxicity of treating colorectal liver metastases with electrochemotherapy. The study is led by Assist. Dr Ibrahim Edhemović, MSc, and coordinated by Prof. Dr Gregor Serša, PhD. Other health professionals employed at the Institute of Oncology Ljubljana and the University Medical Centre Ljubljana, as well as researchers from the Faculty of Electrical Engineering, University of Ljubljana, also be involved in the study.

The study is the continuation of a previous clinical study with the same name, approved by the National Medical Ethics Committee of the Republic of Slovenia on 22 October 2008, and involving a larger number of patients.

It is important that you carefully read and understand this document before signing the consent. The document sets out the purpose, procedures, benefits, risks, possible adverse effects, and precautions related to the study. If you are not completely honest with your doctor about your medical condition, participating in the study may be detrimental to you. ***If this document contains any terms or expressions that you do not understand, please ask your doctor or healthcare professional participating in the study to explain them to you before signing.***

Participation in the study is voluntary and you can refuse to participate. Furthermore, you are free to withdraw from study whenever and without giving a reason – this will not affect your further care or relationship with your doctor at that institution.

Details of the study are described below. It is important that you understand the information provided, as this is the only way you can make an informed decision whether to participate or not. If you decide to participate, you will receive a copy of the signed consent.

What is the purpose of the study?

The purpose of the study is to determine the efficacy of bleomycin-based electrochemotherapy and potential toxicity during surgery on colorectal liver metastases.

Why was I asked to participate in the study?

We suggest treatment of colorectal liver metastases using electrochemotherapy because you have been identified as having one of the following conditions:

a) Colorectal metastases that are not suitable for surgical removal or treatment with standard ablation techniques due to their anatomical position.

b) Progression of the disease in the form of recurring colorectal liver metastases for which another type of treatment would be either risky or expected to be less effective.

c) Colorectal metastases arising simultaneously with the primary tumour. Because your general health does not allow simultaneous surgical removal of both the primary tumour and liver metastases, two surgeries are planned for you according to the standard treatment protocol: removal of the primary tumour during the first operation and removal of liver metastases during the second operation. During the first operation, i.e. when the primary tumour is removed, electrochemotherapy would be used to treat liver metastases because we expect a reduction in their size or their complete disappearance, which would facilitate the second operation or even make it unnecessary.

d) Colorectal metastases for which two operations are planned due to the extent of the disease. During the first operation, the hepatic vein would be ligated to allow the left lobe of the liver to grow to such an extent that by the second operation, the removal of the right liver lobe would be safe (which is not the case now). Some of the metastases on the right liver lobe would be treated with electrochemotherapy during the first operation, while others would not. During the second operation, the right liver lobe would be removed along with all the metastases.
In this case, electrochemotherapy treatment would not affect the course of the disease; your treatment would be in line with the standard protocol, completely uninterrupted and unchanged. By analyzing the electrochemotherapy-treated metastases, we would gain new information and knowledge that would help future patients with the same disease.

How long will the cooperation last?

Your participation in the study, including the screening period, will last approximately **4 months**.

How will the treatment take place?

You will receive treatment while under general anaesthesia. The treatment involves an intravenous injection of the chemotherapeutic agent bleomycin and, after approximately 8 minutes, application of electrical pulses via sterile stainless-steel electrodes inserted into the metastases.

Appointments and procedures during the study:

During the study, you will have at least **7 appointments** over a period of **4 months**.

The treatment consists of the following:

→ **1st appointment: screening (up to 2 weeks before treatment)**

If you agree to participate in the study, your doctor will examine you to see if you are a viable candidate. You and your doctor will also discuss any previous illnesses and treatments.

The examination will consist of the following.

- General medical examination: measuring the electrical activity of the heart (ECG).
- Venous blood collection for haematological and biochemical examinations and coagulation tests.

- Radiological examinations: you will be referred to computed tomography with perfusion (CT perfusion), dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) or dynamic contrast-enhanced ultrasound (DCE-US).
- You will complete a quality-of-life questionnaire.

→ **2nd appointment (1 day before treatment)**

- General medical examination: measuring the electrical activity of the heart (ECG).
- Venous blood collection for haematological and biochemical examinations and coagulation tests.

→ **3rd appointment (1 week after treatment)**

- General medical examination.
- Venous blood collection for haematological and biochemical examinations and coagulation tests.
- You will complete a quality-of-life questionnaire.

→ **4th appointment (1 month after treatment)**

- General medical examination.
- Venous blood collection for biochemical analysis.
- Radiological examinations: you will be referred to CT perfusion, DCE-MRI or DCE-US.
- You will complete a quality-of-life questionnaire.

→ **5th appointment (2 months after treatment)**

- General medical examination.
- Venous blood collection for biochemical analysis.
- Radiological examinations: you will be referred to DCE-US.

→ **6th appointment (3 months after treatment)**

- General medical examination.
- Radiological examinations: you will be referred to DCE-MRI.

→ **7th appointment (4 months after treatment)**

- General medical examination.
- Venous blood collection for biochemical analysis.
- Radiological examinations: you will be referred to CT perfusion and DCE-US.

What are the potential benefits of the study for me?

Electrochemotherapy is used as a standard method to treat cutaneous tumours. Our experience gained from having treated 16 patients also shows the effectiveness of electrochemotherapy in treating liver metastases.

We cannot guarantee that the treatment will be effective in your case, but we hope that we will achieve at least a reduction in the size of the metastases.

What are the potential risks or adverse effects associated with the study?

As with any medicine or treatment, adverse effects may occur during treatment, so we cannot guarantee that you will not experience any adverse effects during the study.

It is important that you inform the doctor monitoring you during the study of any symptoms or a new medicine prescribed by another doctor.

What are my responsibilities if I decide to participate in the study?

You will need to sign a consent form for participating in the study.

You will need to visit your medical institution at least 7 times and undergo the treatments and procedures described in this document.

You will not be allowed to participate in another study while participating in this one.

Before taking any medicine that you have not taken before, you will need to consult the doctor monitoring you during the study.

You will need to report any changes in your general well-being to the doctor monitoring you during the study.

What are my options if I choose not to participate in the study?

If you do not wish to participate in this study, you will continue to be treated by your doctor. Your health care and treatment will not be compromised. You are free to withdraw from study at any time. Doing so will not affect your further medical care.

What if new information becomes available during the study?

Sometimes, new information about the treatment in question comes up during the study. In this case, your doctor will inform and discuss with you whether you wish to continue participating in the study. If you decide to withdraw from the study, your doctor will offer you other treatment options. If you decide to continue participating in the study, you will be asked to confirm your continued participation in the study by signing an updated consent form.

How will my privacy be protected?

In this study, your personal information and information about your medical condition will be documented anonymously (without your name, using only the number you will be assigned upon entering the study).

In accordance with Slovenian legislation, all data collected during the study will be kept strictly confidential. The results of the study, including photographs of tumour lesions, will be available for scientific evaluation purposes and will be published anonymously in health publications.

Voluntary participation and termination of participation:

Participation in the study is voluntary. You can choose to withdraw from the study at any time. Doing so will not affect your current or future medical care. To withdraw from the study, please contact Assist. Ibrahim Edhemović, MD, MSc, on +386 1 5879 953.

Please note that if you withdraw from the study, your doctor will still be able to use the information gathered while you were still part of the study.

Your participation in the study may be terminated without your consent if you fail to follow the instructions and protocol. Further, we may exclude you from the study without your consent if the treatment being studied is detrimental to you and has adverse effects.

Will I need to pay to participate in the study?

The treatment is free of charge.

Who may I contact if I have a question about harm or a reaction associated with the study?

You have the right to ask questions about the study and to have them answered.

If you have any questions about participating in the study or think that you have been harmed in the study or that you have a reaction to the treatment being tested, please contact:

Assist. Ibrahim Edhemović, MSc, MD by phone: +386 1 5879 953 or by email: iedhemovic@onko-i.si

Who may I contact to report a breach of data protection policy:

If you believe that there has been a breach of your personal data, please contact the principal investigator:

Assist. Ibrahim Edhemović, MSc, MD by phone: +386 1 5879 953 or by email: iedhemovic@onko-i.si

Who may I contact if I have a question about my patient rights?

The study has been reviewed and approved by the Committee for Expert Evaluation of Clinical Research Protocols at the Institute of Oncology Ljubljana. If you have questions about your patient rights, you may contact (including anonymously):

Assist. Prof. Cvetka Grašič Kuhar, MD, PhD on +386 1 5879 283 or at

cgrasic@onko-i.si

Patient consent for participating in the study

- I, the undersigned, hereby agree to participate in the study "Treating liver metastases using electrochemotherapy". I understand that my refusing to participate in the study will not affect my health care.
- I have read the description of the study. The study and the starting points have been explained to me in language I understand. I am aware that participation is voluntary. I am sufficiently familiar with the purpose, methods, risks and benefits of the study.
- I understand that the doctor in charge of the study will inform me of any new findings that have arisen during the study that may affect my consent.
- I allow my study-related medical information to be used and passed on to health authorities and institutions. I consent to the use and disclosure of my personal health information as described in this document.
- I understand that I may refuse to participate in the study. I further understand that I am free to withdraw from the study at any time and without giving a reason, and that this will not affect my further care or relationship with my doctor.
- I declare that I have read this document, have had the opportunity to ask as many questions as I wanted, and have received satisfactory answers thereto. I understand that I have not waived any legal rights I have as a participant in the study.
- I am aware that I will receive a copy of the signed voluntary consent.
- I allow samples of metastases to be stored for histological analyses, and photographic records to be published for scientific purposes.

  ❒ Yes ❒ No

I have read the whole document. I have asked all the questions I had. I agree to participate in this study.

Name of the patient/subject in block letters

Signature of the patient/subject | Date (*DD/MM/YYYY*)

Name of the person obtaining the consent in block letters

Signature of the person obtaining the consent | Date (*DD/MM/YYYY*)

Name of the person responsible for the study in block letters

Signature of the person responsible for the study | *Date (DD/MM/YYYY)*