Hannover Medical School

PATIENT INFORMATION AND DECLERATION OF CONSENT

on the study entitled

„A randomized clinical trial comparing laparoscopic or robot-assisted radical/simple hysterectomy versus abdominal radical/simple hysterectomy in patients with early-stage cervical cancer“

Short title

German-funded Laparoscopic Approach to Cervical Cancer (G-LACC)

Address of study site: **<individual data>**

Clinic
Department
Street No.
PLZ City

Phone number:

_____

Investigator:

_____

_____

Dear Patient,

You have been diagnosed with early-stage cervical cancer and are now being considered for surgical treatment. We would like to invite you to participate in this study on surgical treatment of early cervical cancer. The project is fully supported and funded by the German Cancer Aid (Deutsche Krebshilfe - DKH). You can find the detailed information about this study below.

Why is this study being conducted?

Cervical cancer is the fourth most common cancer in women worldwide and mainly affects young women. The standard treatment for early-stage cervical cancer is removal of the entire uterus, the upper part of the vagina, part of the holding apparatus, and the associated lymph nodes. Originally, the surgery was performed via an abdominal incision (abdominal radical hysterectomy). In recent decades, minimally invasive surgery (laparoscopic hysterectomy) has become increasingly popular, requiring only three to five small, keyhole-sized incisions. Studies have shown that minimally invasive surgery is associated with less blood loss, a shorter hospital stay and fewer complications.

The background of the planned G-LACC study is the surprising result of a recent study (LACC trial) comparing both approaches. The LACC trial showed decreased survival rates for the minimally invasive approach. The study results led to a wide discussion in gynecological oncology and contributed to the decision of many gynecologists to stop offering minimally invasive surgery. However, due to the lack of standardized surgical techniques and quality criteria in the above-mentioned trial, many experts question the study results. In particular, it is criticized that the minimally invasive group in this study used a technique to remove the uterus that could potentially spread tumor cells in the abdomen. Subsequently, there have been numerous other evaluations, albeit of lesser scientific significance, that have partly confirmed and partly contradicted these results. In particular, large European trials have demonstrated that certain “protective measures” taken during surgery to prevent the spread of tumor cells can result in comparable cure rates after minimally invasive surgery compared to open surgery. Therefore, in order to continue to offer patients the benefits of minimally invasive surgery, another comparative study with clearly predefined surgical techniques to prevent tumor cell spread is urgently needed. The main objective of our G-LACC study is to demonstrate that minimally invasive surgery is not inferior to open

surgery in terms of survival, considering the aforementioned “protective measures”. Further analyses will include the quality of life of the participants, complications and adverse events.

What makes this study stand out?

This study focuses on your safety. Therefore, strict quality requirements are set for the participating centers. Surgery is performed using the latest knowledge to avoid tumor cell spread during surgery. In a strict selection process, the surgical quality of your hospital has been evaluated by a committee of experts and confirmed to meet the quality requirements.

What is being examined?

This study investigates two different surgical techniques:

- Open surgery (abdominal radical/ simple hysterectomy)
- Minimally invasive surgery (laparoscopic or robot-assisted radical/ simple hysterectomy).

Whether the open or minimally invasive technique is applied to you is decided randomly. You will be informed of the outcome of this randomization before the operation.

Is participation voluntary?

Of course, participation in this study is voluntary and you can withdraw at any time without giving a reason and without any consequences for your further treatment.

How does the study work?

If you agree to participate in the study after adequate information and sufficient consideration, you will be assigned to one of the two treatment groups using a structured randomization process. This randomization allows for the best possible equal distribution between the two treatment groups and thus provides the most robust results for a scientific study. In both treatment arms, removal of the uterus with holding apparatus, removal of the portion of the vagina adjacent to the uterus, and removal of the pelvic lymph nodes (as a sentinel lymph node procedure, if necessary) is performed. In the minimally invasive arm, 3-5 punctures (1-2cm) are used to perform

the surgery and the uterus is retrieved through the vagina using the prescribed “protective measures” to prevent the spread of tumor cells.
If you have a tumor less than 2cm in size and it still meets certain criteria, a simple hysterectomy can be performed in consultation with your doctor.
If the operation reveals more extensive findings than previously thought (larger tumor, lymph nodes affected), the study will be terminated for you, but treatment will continue according to national guidelines.
After surgery, you will be followed up, according to the protocol, at one and six months and annually until the fifth year after surgery. During the follow-up appointments, you will be asked to complete questionnaires about your current quality of life in relation to your disease. In addition, your investigator will ask you about any potential problems and may take blood samples and/or swabs. Follow-up care will be in accordance with the national guideline for the diagnosis and therapy of cervical cancer.

What are the health risks and burdens associated with participation?
Both surgical techniques involve operational risks, which are listed below. However, according to current recommendations, surgery is the first-line therapy for early-stage cervical cancer. In the largest study comparing the two surgical approaches (LACC trial), there was no long-term difference in surgical complications between the two procedures. In contrast, other studies showed that the minimally invasive approach was associated with less blood loss, faster mobilization and fewer postoperative complications. In general, both procedures carry the following risks:

- Injury to neighboring organs: organs such as the bladder, intestine, ureter, urethra, or nerves may be injured during the operation, which may cause further operations or late effects.
- Bleeding: Bleeding of varying severity may occur during surgery and can usually be stopped quickly. In rare cases, an extension of the operation, a new operation or the administration of blood products are necessary.
- Urinary retention: After surgery, it may not be possible to empty the bladder. This has become much less common with nerve-preserving surgical techniques. In some cases, a bladder catheter must be left in place for a longer time.

- Infections: Bacteria can enter the wound regions because of the surgery and infections can occur. In rare cases, a secondary surgery must be performed. Usually antibiotic therapy is sufficient.
- Blood clots: Due to the surgery and prolonged immobilization, there is an increased risk of blood clots (thrombosis). These can develop into displaced blood clots (embolisms) in the lungs or brain, which can have long-term effects. Therefore, you will be encouraged to move early after the surgery and receive medication to prevent thrombosis.
- Wound healing disorders: Depending on the size of the scars and possible pre-existing conditions, wound healing disorders may occur. In rare cases, this can lead to an abdominal wall hernia, which may need to be operated on again.
- Skin/ soft tissue/ positioning damage: Because of the operation and the positioning during the operation damage (tissue death, hematoma, swelling, nerve injury) may occur which may also have long-term consequences (numbness, insensitivity, scars). The staff in the operating theater will keep a close eye on your positioning during the operation.
- Infertility: Pregnancy is not possible after removal of the uterus. The ovaries are usually left in place to maintain hormonal function. Due to the removal of the uterus, there is a risk that menopause will occur earlier than normal.
- Lymphedema: Removal of lymph nodes increases the risk of infection, lymphatic fluid accumulation (seroma) and edema (accumulation of water within tissues). This can lead to permanent impairment. Additional surgeries may be required. Sentinel lymph node removal can reduce the risk of these side effects occurring.
- Recurrence: Tumor recurrence depends on many factors and can be reduced by optimal surgical procedures. The large LACC trial showed that 86% of patients were tumor-free after minimally invasive treatment, while 96.5% were tumor free after open surgery. This was also confirmed in overall survival (minimally invasive 93.8% versus open 99.0%). Further publications demonstrated similar results. However, numerous other publications showed that when surgical techniques were used to prevent distribution of tumor cells in the abdomen, the minimally invasive procedure achieved similarly safe results as open surgery. Similarly, in cases where the tumor had already been removed by means of a conization prior to removal of the uterus, there was no

increased risk of recurrence due to minimally invasive surgery. Therefore, this study prescribes surgical measures to prevent the likelihood of a distribution of tumor cells after minimally invasive surgery.

If the applied technique leads to a higher rate of recurrence of tumors despite the measures taken to prevent tumor cell distribution, this procedure may reduce your chances of recovery.

What personal benefit do I get from participating in the study?

In the open treatment arm, you will receive the standard therapy as recommended from national guidelines. Based on the results of the LACC study, this approach is associated with an improved survival rate.

If you are assigned to the minimally invasive treatment arm, you may benefit from faster recovery after surgery, less blood loss, and fewer postoperative complications. It is not yet known which of the two methods is better and whether there is any additional benefit for you. This is the subject of the trial.

Who is not allowed to participate in this clinical trial?

Pregnant women are not allowed to participate in this clinical trial. Therefore, all women must undergo a pregnancy test prior to the clinical trial. Women who can no longer become pregnant are exempt from this requirement (e. g. after menopause).

What other treatment options are available outside of the study?

Surgical treatment with radical/ simple hysterectomy and (sentinel) lymph node removal is the recommended first-line treatment of early-stage cervical cancer. If you are not enrolled in this trial, your clinic will recommend the same treatment to you. In this case you will either receive therapy as recommended in current guidelines or therapy according to an individual approach.

Will there be any costs involved in taking part in the study? Will I receive an expense allowance?

There will be no financial compensation for your participation in this study. There are no additional costs for you.

Will I be insured during the clinical trial?

As with any hospital stay, you are covered by the professional liability insurance of the clinic during the study. If you suspect that participation in the study has damaged your health or aggravated existing conditions, please contact your doctor immediately.

As part of the G-LACC study, a group accident insurance policy has been taken out. The insurance covers accidents that occur during your stay at the study center for the purpose of the study.
Direct travel to and from the study center is also covered. The insurance does not cover any unnecessary extension of the trip or if the trip itself is interrupted by purely private and independent activities (e.g. shopping, visiting restaurants for private purposes).
A copy of the insurance policy can be obtained from your doctor at the center upon request.

In case of damage, please contact the insurance company immediately:

Name/Address of insurance company: SV Sparkassen Versicherung
Gebäudeversicherung AG

Phone:
Fax:

Policy-ID:

If necessary, ask your study doctor for assistance in order not to jeopardize your insurance cover. If your doctor is supportive, you will receive a copy of the report. If you send your claim directly to the insurer, please also inform your study doctor.

What happens to the data collected about me?
The legal basis for data processing is your informed consent in accordance with Article 6 para. 1 letter a, and Article 9 para. 2 letter a of the GDPR (General Data Protection Regulation).

The person responsible for data processing is:

Prof. Dr. Peter Hillemanns,
Clinic for Gynecology and Obstetrics (OE 6410)
Carl-Neuberg-Str. 1, 30625 Hannover

The data will be treated confidentially at all times. The data will be forwarded in a pseudonymized format to the initiator of the study, the Hannover Medical School, or to agencies commissioned for the purpose of scientific evaluation. Only the responsible persons in the respective study center have access to the personal data.
Pseudonymization means that the personal data, such as the name and date of birth, can no longer be assigned to a specific person without consulting a special identification list. The personal data is replaced by a number and/or letter code; the date of birth is limited to the year of birth. Such a list is stored in the study center, where the names are assigned to the number and/or letter codes. This list is kept separately at the study center and is highly protected to ensure that the personal data cannot be assigned to you by unauthorized persons.
The data are retained for 15 years after the end of study or discontinuation. They are secured against unauthorized access. They are deleted after 15 years at the latest.
Competent employees of the initiator of the study or companies commissioned for the purpose of scientific evaluation who are bound to secrecy (for further details, please refer to the data protection consent form) may inspect the treatment records available at the study center in order to check the data transmission. With your signature, you release your physicians from the medical confidentiality obligation for this purpose.

Are there any risks associated with data processing?

Confidentiality risks (e.g., the possibility of identifying the person concerned) exist whenever data is collected, stored, used and transmitted. These risks cannot be completely ruled out. The initiator of the study assures you that everything possible will be done according to the state of the art to guarantee that data will only be passed on to organizations that can demonstrate an appropriate data protection concept. No medical risks associated with data processing.

Can I revoke my consent?

You may revoke your respective consent in writing or verbally at any time without giving reasons and without incurring any disadvantage. If you revoke your consent, no further data will be collected. However, the data processing that took place until the revocation remains lawful.

What other rights do I have with regard to data protection?

With regard to your data, you have the following rights in accordance with Article 13 et seq. of the GDPR:

Right to information:

You can request information about the relevant personal data collected, processed or transmitted to third parties in the context of this study at any time (Article 15 GDPR).

Right to rectification:

You have the right to have inaccurate personal data concerning you corrected (Articles 16 and 19 GDPR).

Right to erasure:

You have the right to request the erasure of your personal data, e.g. if this data is no longer necessary for the purpose for which it was collected (Articles 17 and 19 GDPR).

Right to restriction of processing:

Under certain conditions, you have the right to request the controller to restrict processing, i.e. the data may only be stored, not processed. You must request this. Please contact your study doctor or the data protection officer of the study center (Articles 18 and 19 GDPR).

Right to data portability:

You have the right to receive the relevant personal data that you have provided to the controller for this study. This means that you can request that this data be transferred either to you or, if technically possible, to another body designated by you (Article 20 GDPR).

Right to object:

In principle, you also have a general right to object to lawful data processing that is carried out in the public interest, in the exercise of official authority or on the basis of the legitimate interest of a body (Article 21 GDPR).

As a rule, please contact your study site, because only the staff at the study site can fully access your data or provide corresponding information due to the pseudonymization process. The initiator of the study can therefore only be of limited help.

If you have any concerns about data processing and compliance with data protection requirements, you can also contact the following data protection officers:

Data Protection Officer of the Study Center:

Clinic

Data Protection Officer:

Street No., PLZ City

E-Mail:

Data Protection Officer of the Responsible Investigator:

Hannover Medical School

Data Protection Officer of the MHH – OE 0007

Carl-Neuberg-Straße 1, 30625 Hannover

Datenschutz@mh-hannover.de

You have the right to complain to any data protection authority. You can find a list of the supervisory authorities in Germany at:

https://www.bfdi.bund.de/DE/Infothek/Anschriften_Links/anschriften_links-node.html

Who do I contact if I have further questions?

You will always have the opportunity for further consultation with the investigator named on page 1 or any other investigator.

Study site: **<enter name of study site>**

Study doctor: _____

Name in Druckbuchstaben

DECLERATION OF CONSENT

as part of the study

„A randomized clinical trial comparing laparoscopic or robot-assisted radical/simple hysterectomy versus abdominal radical/simple hysterectomy in patients with early-stage cervical cancer“

Patient's name in block letters: _____

Date of birth: _____ Participant No: _____

- I have been informed by Mrs. / Mr. _____ about the nature, significance and scope of the study as well as the resulting requirements for me. I have also read the text of the patient information and this declaration of consent.
- I had sufficient time to ask questions and make a decision. Any questions that arose were answered by the study doctor.

Space to document additional questions from the patient or other aspects of the consultation:

_____

_____

_____

_____

_____

- I know that I can terminate my voluntary participation at any time without incurring any disadvantages.

Consent under data protection law

I am aware that personal data, in particular medical findings about me, will be collected, stored and analyzed in this study. The use of the information about my health is carried out in accordance with legal regulations and requires the following voluntary declaration of consent before participation in the study, i.e. without the following consent I cannot participate in the study.

1. I consent to personal data about me being collected as described in the information sheet and recorded in paper form and on electronic data carriers in the study center (see page 1). For this purpose, I release the doctors treating me from their duty of medical confidentiality. As far as necessary, the collected data may be forwarded pseudonymized (encrypted):

a) to the Hannover Medical School or to bodies commissioned by it for the purpose of scientific evaluation,

b) in the case of adverse events: to Hannover Medical School, to the relevant ethics committee and competent authorities and from there to the European database.

2. Furthermore, I agree that authorized representatives of the initiator of the study, who are bound to secrecy, may inspect the treatment records of my attending physician, insofar as this is necessary to verify the data transfer. For this measure, I release the physicians involved from their duty of confidentiality.

3. I have been informed that I can withdraw my consent at any time. In the event of revocation, no further data will be collected. In this case, I can request the deletion of the data.

4. I agree that the data will be stored for at least 15 years after completion or discontinuation of the clinical study.

I agree to participate in the study voluntarily.
At the same time, I consent to the processing of the aforementioned data.

I have received a copy of the patient information sheet and the declaration of consent. One copy remains at the study site.

Signature of the patient

_____
(Patient's name in block letters)

_____ _____
(Place, date – to be entered by the patient) (Patient's signature)

Declaration and **Signature of the Physician providing the information**

I conducted the informed consent interview and obtained consent.

_____
(Doctor's name in block letters)

_____ _____
(Place, date) (Signature of the informing study doctor)