Patient-ID: □□-□□□-□□□

AXSANA

A prospective multicenter cohort study to evaluate different surgical methods of axillary staging (sentinel lymph node biopsy, targeted axillary dissection, axillary dissection) in clinically node-positive breast cancer patients treated with neoadjuvant chemotherapy

Patient Information:

Dear Patient,

We would like to invite you to take part in the AXSANA study.

You have been diagnosed with breast cancer and your doctor has informed you that it had spread to the lymph nodes in your axilla (armpit). You have already discussed with your doctor the possibility of neoadjuvant chemotherapy (i.e. chemotherapy before surgery).

Chemotherapy administered before surgery leads to shrinking of the tumor mass in most patients and, in approximately 40% of patients, to successful elimination of tumor cells from the lymph nodes. In such case, no vital tumor cells are found in the lymph nodes removed at surgery after chemotherapy.

Your doctor will discuss with you which form of axillary surgery will be recommended after chemotherapy. Your participation in our study does not influence the choice of therapy in any way.

Several different forms of surgical therapy of axilla are currently used in order to determine whether the tumor spread to the lymph nodes or not. The classical technique is called “axillary lymph node dissection”, where all or most lymph nodes are removed from the armpit. New techniques have been developed to lower the number of removed nodes and reduce long-term complications such as lymphedema (swelling of the arm). So far, studies have shown that the surgery can be conducted in a less radical manner in selected patients. In some cases, the metastatic lymph node may be marked before chemotherapy and removed during surgery after localization of the marking. In some cases, a so-called sentinel lymph node may be removed at surgery.

Because it is still a matter of debate which surgical technique is the optimal one, the recommendations in different hospitals and countries differ. The international and national guidelines on axillary surgery differ as well.

Even for patients who still have affected lymph nodes after neoadjuvant chemotherapy, the optimal treatment is controversially discussed. This applies in particular to very small lymph node metastases (so-called micrometastases = metastases with a size < 2 mm). It is currently unclear whether in these cases complete axillary lymph node dissection, radiation or no specific treatment of the lymph nodes is required. Due to inconclusive evidence, recommendations differ across hospitals and countries.

Therefore, we decided to collect patients' data in a prospective registry to evaluate the success rate and feasibility of different surgical techniques. The cohort study AXSANA has been initiated by the EUBREAST e.V study group (European Breast Cancer Research Association of Surgical Trialists) and is currently being conducted in several European countries. EUBREAST is a non-profit network of renowned oncological breast surgeons and aims at joining forces throughout Europe to accelerate scientific progress for the direct benefit of breast cancer patients (www.eubreast.com).

If you agree to participate in the AXSANA study, the data regarding your tumor stage, results of imaging and histological examinations, therapy details, follow up and quality of life will be registered within the study. Your therapy will be conducted according to the current standards of your treating institution and will not be altered due to study participation in any way.

We would like to ask you for your permission to register your treatment data. If your histological and/or operation reports are forwarded to the study organizers, your personal data will always be pseudonymized (i.e. all personally identifiable information will be replaced by a number code and your year of birth, without using your initials). By participating in this study, you will help to clarify which surgical technique is most suitable for patients in your situation.

Course of the study:

The participation in this study will not influence your treatment in any way. Your doctor will discuss the therapy with you as part of routine clinical practice.

The following routine data will be registered if you participate in the study:

- Tumor details such as tumor size, number of suspicious lymph nodes and tumor subtype

- In case the lymph node(s) was/were marked prior to start of therapy: type of marking and number of marked nodes
- Type and duration of chemotherapy
- Tumor response and response of lymph nodes to chemotherapy
- Type of surgery and histological results
- Therapy following surgery
- Follow up data

In addition, you will be asked to complete standardized quality of life questionnaires.

What does study participation mean?

Your participation in the AXSANA study allows the registration and evaluation of your therapy details. The study is aimed at analyzing different surgical techniques and their impact on the course of disease and patients' quality of life. Further, different methods for lymph node marking will be evaluated.

Breast cancer patients will be invited to participate in the study at several study sites. The study aims to register data of as many patients as possible from different European countries. Personally identifiable information will not be shared or published. All treatment-related decisions will be discussed with you by your treating doctor. These decisions are not influenced by your study participation in any way.

Your participation in the study and the analysis of treatment-related data will hopefully help to clarify which surgical technique is most beneficial for breast cancer patients undergoing neoadjuvant chemotherapy. The participation in this study is voluntary. Withdrawing from the study is possible at any time without stating any reason and has no disadvantages for the further medical care.

Who can participate in the study?

The AXSANA study has following inclusion and exclusion criteria:

<u>Inclusion criteria</u>

- Signed informed consent form
- Invasive breast cancer (confirmed by core biopsy)
- Tumor spread to lymph nodes in the armpit
- Tumor stage cT1 to cT4c

- Planned chemotherapy before surgery
- Female / male patients ≥ 18 years old

Exclusion criteria

- Tumor spread to distant organs (distant metastasis)
- Recurrent breast cancer
- Inflammatory breast cancer
- Breast cancer located outside the breast
- Breast cancer of both breasts
- History of invasive cancer of the breast or other organs or ductal carcinoma in situ
- Tumor spread to lymph nodes located over the clavicle or beside the sternum
- Surgery of the armpit before begin of neoadjuvant chemotherapy
- Pregnancy
- Less than 4 cycles of chemotherapy administered before surgery
- Patients not suitable for surgical treatment

Are there any expenses for the participants?

There are no expenses for the participants in this study.

Will the data collected in this study be protected?

Your medical and personal data will be recorded in your medical files. Some of the data will be registered using paper and/or electronic questionnaires. Only pseudonymized data will be shared with the study center (i.e. all personally identifiable information will be replaced by a number code and your year of birth, without using your initials). The data will be shared solely for statistical purposes. You will never be mentioned by name. In publications of the data of this study, you will not be mentioned by name.

Clinical trial insurance:

The AXSANA study is a registry-based cohort study and does not include any study-specific therapies. Therefore, trial insurance is not required.

Who has approved the AXSANA study?

The study has been approved by an independent ethics committee.

Analysis of benefits and risks of the study

No risks are associated with participation in this study. There will be no benefit for the individual patient participating in this study.

Who is funding the study?

The financial support for this study has been provided by the following institutions: AGO-B study group, AWOgyn (The Working Group for Reconstructive Surgery in Oncology-Gynecology) and Claudia von Schilling Foundation for Breast Cancer Research. Further support may be applied for.

Data protection

Data will be protected under the The Prevention of Electronic Crimes Act of Pakistan, 2016
Other personnel and institutes involved are:

- Responsible for data management: EUBREAST e.V., represented by Prof. Dr. med. Thorsten Kühn, 1. Chairman, Baumreute 37, D-73730, Esslingen, Deutschland, E-Mail: info@eubreast.com.
- Data protection officer for EUBREAST e.V.: Dr. Marina Mangold, Esculape, Marktstraße 17, 35075 Gladenbach, datenschutz-eubreast@esculape.de
- All data are pseudonymized
- All data are analyzed by EUBREAST e.V. or other commissioned institutions, but data never leave the EU
- The quality of life analysis will be performed by the Karolinska Institutet in Sweden.

Contact person:

In case of any questions you may contact: Dr Anum Wahid

Study site:
Khyber Teaching Hospital, Peshawar, Pakistan

Head of the National Steering Committee:
Xxxxxxx

International Study Chair:
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Germany
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For any further questions:

The responsible doctor and his/her team are available for any further questions regarding this study. They will answer all questions you might have in relation to this study.

AXSANA

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Informed Consent Form

Year of Birth: __ __ __ __ **Patient-ID:** ☐☐-☐☐☐-☐☐☐

Name of the patient: _____

Name and address of the study site:

I was informed in detail about the AXSANA study. I have read the text of this patient information and the informed consent. All questions were answered in an understandable and detailed way by the responsible doctor. I agree with the data obtained from the study to be recorded. I had enough time to decide about participating in this study and have no further questions. I have been informed that I can always contact the responsible doctor in case of questions.

I have been informed about my right to revoke my consent for the study without causing any disadvantages for further medical care.

DATA PROTECTION

Please include here a text passage regarding data protection recommended in your country.

Include following information:

- Responsible for data management: EUBREAST e.V., represented by Prof. Dr. med. Thorsten Kühn, 1. Chairman, Beumreute 37, D-73730 Esslingen, Deutschland, E-Mail: info@eubreast.com.

- Data protection officer for EUBREAST: Dr. Marina Mangold, Esculape, Marktstraße 17, 35075 Gladenbach, datenschutz-eubreast@esculape.de
- All data are pseudonymized
- All data are analyzed by EUBREAST or other commissioned institutions, but data never leave the EU
- The quality of life analysis will be performed by the Karolinska Institutet in Sweden.
- All data will be anonymized 10 years after the patient joined the study

I agree to participate in the AXSANA study.

To be completed by the study participant:

Name: _____

Place, date: _____

Signature: _____

To be completed by the responsible doctor / investigator:

I confirm that I have fully informed the participant about the design, purpose and risks of the study as well as further details regarding data transfer and data management in accordance with data protection laws. I confirm that the study participant received the Patient Information and a signed copy of the Informed Consent Form.

Name: _____

Place, date: _____

Signature: _____