

## Sentinel lymph node biopsy in breast cancer patients treated with induction chemotherapy should be performed after the completion of chemotherapy

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Sentinel lymph node biopsy in patients with early breast cancer treated with breast conserving therapy is currently a standard treatment. SLN biopsy allows to resign from the resection of the axillary lymph nodes and thus, to reduce the risk of complications and to improve the quality of life of the patients. The objective of preoperative chemotherapy is to decrease the scope of surgery both within the primary focus of the tumour and in the axillary lymph nodes. The results of the research carried out so far indicate that SLN biopsy, after a preoperative chemotherapy in patients at the N<sub>0</sub> and N<sub>1-2</sub> clinical stage is credible and in allows many of them to avoid the resection of axillary lymph nodes. Therefore there are rational arguments justifying SLN biopsy after the completion of preoperative chemotherapy.

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### Introduction

The sentinel lymph node (SLN) is the first lymph node in the lymphatic drainage of the primary focus of the tumour. It is believed that the SLN is the first site of accumulation of tumour cells at the stage of the occurrence of metastases in the regional lymph nodes [1–3]. The most frequent method of sentinel lymph node identification is preoperative lymphoscintigraphy with the <sup>99m</sup>Tc radionuclide on an aluminium carrier connected with a perioperative staining of lymph drainage with methylene blue. In some centres, in order to increase the sensitivity of SLN identification, hybrid techniques are used i.e. the connection of functional imaging with morphological one (SPECT/CT, single photon emission with a low-dose CT) [4]. During surgery, the lymph nodes with the largest radioactivity and the most stained, which are regarded as SLN are removed. It is admitted that the sensitivity of the SLN biopsy should be above 90% with the rate of false positive results below 10%. The improvement of the rate of identified SLN is significantly affected by the number of procedures performed by the surgeon, i.e. their experience and practice [5–7].

Preoperative (induction) chemotherapy in breast cancer patients is used in order to decrease the advancement stage of the primary tumour and/or lymph nodes, which allows for a breast conserving procedure. In more advanced cases (T4, N2–3 stage), preoperative chemotherapy may facilitate or make possible a radical surgery procedure [8]. Currently, in patients with so-called aggressive phenotypes, which at the same time are characterised with high sensitivity to chemotherapy and/or molecularly targeted treatment (triple negative cancer and HER2-positive), the induction treatment is also often applied in patients in the N0 stage if the tumour's diameter is larger than 2 cm [8, 9]. In these phenotypes, the rate of pathologic complete response (pCR,) affects the improvement of survival parameters [9].

### Radiotherapy vs axillary lymphadenectomy in patients in the N0 clinical stage and a metastasis in a sentinel lymph node

In 3 prospective clinical trials (ACOSOG Z0011, AMAROS, IBCSG 23-01) it was shown that in patients with metastases

in the SLN, the resection of axillary lymph nodes can be avoided. The ACOSOG Z0011 study compared the treatment with and without axillary lymphadenectomy in patients treated with the BCT and post-operative radiotherapy with tangential fields; this led to the conclusion that in the case of metastatic involvement of 1 or 2 SLN, the rate of loco-regional recurrences, the time to progression and the overall survival periods, are similar after 5 years, in spite of the fact that in the group undergoing axillary lymphadenectomy in about 30% patients, the metastases to consecutive lymph nodes were found [10]. The AMAROS study showed that axillary irradiation is equally effective as surgery with a much lower risk of complications [11]. Similar results were rendered by the IBCSG 23-01 study which concerned patients with micro-metastases in SLN [12].

### Preoperative chemotherapy in patients at the N0 clinical stage

Before the commencement of preoperative chemotherapy in patients at the cN0 stage, a number of additional tests must be performed, including an ultrasound of the axilla, connected, when metastases are suspected, with a biopsy of axillary lymph nodes and also to mark the primary tumour with clips or a tattoo. In some centres, in order to evaluate the advancement stage, additionally a breast MRI or position computed tomography (PET/CT) is performed. Postponing the SLN biopsy until the moment of completion of preoperative chemotherapy does not significantly reduce the accuracy of the examination; the rate of identified SLN in this group is more than 90%, and false negative results concern 6–9% of patients [13–15]. That is why, international guidelines, including those from the most recent conferences on the treatment of early breast cancer — St. Gallen, recommend the SLN biopsy in patients at the N0 stage after the completion of preoperative chemotherapy [8, www.oncoconferences.ch/BCC].

### Preoperative chemotherapy in the patients at the N+ clinical stage

In the case of diagnosing clinical cN+ stage and its confirmation with a fine needle biopsy, there is no need to perform an SLN biopsy before preoperative chemotherapy, as this procedure is performed solely in patients without pathological or clinical symptoms of metastatic involvement of axillary lymph nodes. Regardless of the above, SLN biopsy before preoperative chemotherapy would not change the clinical stage and thus would not affect the choice of the type of surgical intervention, but it would increase the risk of complications and diagnostic costs. It must be remembered that the main objective of preoperative chemotherapy, apart for guaranteeing the possibility of BCT, is to avoid axillary lymphadenectomy. A few studies have shown that the pCR rate within the lymph nodes after preoperative che-

**Table I.** pCR rate within the lymph nodes after preoperative chemotherapy

Study	N	The rate of pCR in the lymph nodes
ACOSOG Z1071 (cT0–4N1/2) <sup>16</sup>	649	41%
SN FNAC (cT0–3N1/2) <sup>17</sup>	145	35%
Mamtani (cT0–3N1/2) <sup>18</sup>	195	49%

motherapy, especially in the following phenotypes: triple-negative and HER2-positive, amounts to 40–50% [16–18] (Tab. I). What is important, axillary lymphadenectomy may be avoided in about 50% of patients with SLN biopsy, confirmed with pCR, after pre-operative chemotherapy especially that the majority of them, an account of the baseline metastatic involvement of the axillary lymph nodes, will undergo radiotherapy of the nodal fields [8, 16–18] (www.oncoconferences.ch/BCC). This fits to the generally accepted tendency to limit axillary lymphadenectomies in breast cancer patients [www.oncoconferences.ch/BCC]. What is more, in spite of earlier concerns about SLN identification after preoperative chemotherapy and the high risk of false negative results, a prospective analysis of the ACOSOG Z1071 and SENTINA studies, has shown that the sensitivity of the SLN biopsy in the case of the removal of at least 3 SLNs is larger than 90%, and the rate of false negative results fits in the range of 10% [19, 20].

### Summary

Preoperative chemotherapy is used mostly with the intention of reducing the scope of a surgery, also in relation to the axillary lymph nodes. The results of the studies carried out so far show that SLN biopsy after preoperative chemotherapy is a reliable method, allowing, in a large group of patients, to avoid axillary lymphadenectomy. Such a possibility is not guaranteed by SLN biopsy before the commencement of preoperative chemotherapy. As a consequence, currently the SLN biopsy after the completion of chemotherapy is becoming a standard treatment method, irrespective of the baseline status of the axillary lymph nodes [8, 19–21, www.oncoconferences.ch/BCC].

**Conflict of interest:** none declared

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