

429

Poster

### Circulating Tumour Cells Before and After Neoadjuvant Chemotherapy in Patients with Primary Breast Cancer

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**Background:** Circulating tumor cells (CTCs) are isolated tumor cells disseminated from the site of disease in metastatic and/or primary cancers that can be identified and measured in the peripheral blood of patients.

**Patients and Methods:** Blood (7.5 ml) was collected from 71 patients with stage II/III breast cancer before neoadjuvant chemotherapy (NAC). NAC consisted of anthracycline and paclitaxel chemotherapy and additional trastuzumab treatment for patients with HER2-positive tumors.

**Results:** One or more CTCs were detected in 15 (21%) of 71 patients. 14 (93%) of 15 CTC-positive patients were negative after NAC. CTCs were detected in 6 (15%) of 39 patients with clinical stage II disease and 9 (28%) of 32 patients with clinical stage III disease. According to tumor subtypes, CTCs were detected in 5 (23%) of 22 patients with hormone receptor (HR)-positive and HER2-negative tumors, 2 (14%) of 22 patients with HR-positive and HER2-positive tumors, 4 (29%) of 14 patients with HR-negative and HER2-positive tumors, and 4 (19%) of 21 patients with HR-negative and HER2-negative tumors (TN). 23 (32%) of 71 patients had a pathologic complete response (pCR) after NAC. There was no correlation between CTC and pathological response. At the median follow up of 24 months, distant metastasis was observed in 6 patients (8.5%). Patients with clinical stage III, triple negative subtype, or non-pCR had a significantly worse disease-free survival. However there was no significant difference of disease-free survival between CTC-positive and negative patients.

**Conclusion:** CTC positivity rate was low in patients with primary breast cancer. CTCs number decrease after NAC irrespective of tumor subtypes.

430

Poster

### The Negative Predictive Value of Sentinel Lymph Node Following Neoadjuvant Chemotherapy in Patients with Positive Pre-treatment Axillary Nodes.

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**Introduction:** Axillary lymph node status is a highly deterministic prognostic factor in breast cancer. In recent years, sentinel lymph node biopsy (SLNB) has replaced conventional axillary lymph node dissection (ALND) for predicting axillary lymph node status with high accuracy. While SLNB has become the standard of care in early operable breast cancer, the role of SLNB in the context of neo-adjuvant chemotherapy (NACT) is still controversial. A number of recent studies have evaluated the feasibility (detection rate) and accuracy of SLNB after NACT in breast cancer patients and suggested that SLNB following NACT is feasible and valid. The aim of our study was to evaluate the negative predictive value of SLNB after NACT in patients with pre-treatment positive nodes. We report the results in patients treated at a single institution.

**Materials and Methods:** 140 patients with documented node-positive breast cancer at presentation, diagnosed by either core needle biopsy and FDG uptake on PET-CT, were treated with Anthracycline based NACT at the Sheba Medical Center between 2002 and 2011. Of these, 130 patients underwent formal ALND. Thirty-six patients underwent lymphatic mapping with SLNB. Of those, in twenty-six immediate formal ALND was then performed. Ten patients with a negative SLNB after NACT did not undergo completion ALND, but rather, were put under close follow up (6 months-6 years). Lymphatic mapping and SLN detection was performed using injection of patent blue dye subareolarly.

**Results:** Of the 130 patients who underwent ALND after NACT, 46% were node negative. The average number of nodes examined was 11.2. The accuracy of SLNB was determined by comparing it to the 'gold standard' histological analysis of ALND. In 26 of the patients who underwent SLNB and ALND, the sentinel node identification rate was 96% (PPV-100% NPV-94%). The sentinel node was falsely negative in one case (4%). The follow up study of 10 patients with negative SLNB who did not undergo ALND showed that 9 patients (90%) maintained long term (up to 6 years) remission while one patient had distant recurrence.

**Conclusions:** Axillary lymph node status can be positively downstage by NACT. Therefore it is reasonable and appropriate to examine the role of SLNB in these patients, primarily due to the fact that whole axillary radiation is regularly administered. SLNB performed following NACT in patients with

documented nodal disease at presentation accurately reflects the status of axillary nodes after treatment and may obviate the need for complete ALND with its resultant morbidity. intensified by the planned radiotherapy. Although several studies have suggested that the use of SLNB following NACT is promising, the data are insufficient and further studies on larger patient populations are required to firmly establish the true negative predictive value of SLNB in these settings.

431

Poster

### The Effects of the Body Mass Index (BMI) on Neo-adjuvant Chemotherapy

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**Background:** Several prior studies have identified that obesity influences the effects of chemotherapy or hormone therapy for breast cancer. However, these reports mainly focused on the effects on adjuvant therapy, and little is known regarding those on neo-adjuvant chemotherapy. Therefore, we sought to evaluate the effects of the BMI on neo-adjuvant chemotherapy.

**Materials and Methods:** Two hundred and sixty-nine female patients (aged 50.8±9.7 years) with breast cancer who underwent surgery after neo-adjuvant chemotherapy from April 2000 to October 2011 were enrolled. These patients were categorized into four groups according to the World Health Organization BMI Classification Criteria: underweight, normal, overweight, obese, BMI <20, 20≤BMI <25, 25≤BMI <30, and BMI ≥30, respectively. By definition, the term 'pathological complete response, pCR' pathologically describes no invasive area in a specimen, and the residual intraductal components were also regarded as pCR (Fisher B et al. J Clin Oncol 16:2672-2685, 1998). Statistical analysis was performed using the chi-square test and a logistic regression model.

**Results:** In the clinicopathological features, significant differences were only found in the age between these four groups (p <0.05). There were no significant differences in the pCR rates or pathological response grade between over 25 and over 30 groups and those with aBMI under 25 (p=0.11, OR=0.35, 95% CI=0.09 to 1.27, p=0.11). The other clinical factors: menopausal status, surgical method, axillary lymph node metastasis, and applying taxanes in neo-adjuvant chemotherapy did not show significant differences between these four groups. In the pathological factors, there were significant differences in the ER status (p <0.05, OR=0.19, 95% CI =0.04 to 0.98).

**Conclusions:** Although the ER status showed significant differences, there were no findings regarding the effects of the BMI on the neo-adjuvant chemotherapy. Some reports state that the dose of drugs for obese patients tends to be reduced compared to the amounts calculated based on the patient's body surface area. On the contrary, in the present study, almost all patients received an adequate dose during neo-adjuvant chemotherapy. It is highly probable that this results in obese patients showing no changes in pCR rates.

432

Poster

### Comparison of Efficiency and Side Effect of Adriamycin and Doxorubicin and Adriamycin, Cyclophosphamide and Paclitaxel in Patients with Locally Advanced Breast Cancer Receiving Neoadjuvant Chemotherapy

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**Background:** It is well known that neoadjuvant chemotherapy is acceptable for women with locally advanced breast cancer. It enables the patients who otherwise require mastectomy to give the chance of breast conservation. Furthermore, it gives information of tumor response of chemotherapy. However, it is not achieving consensus that what kind of regimen is most effective and least adverse effect, although lots of regimens and dosages were clinically used.

**Materials and Methods:** We compared retrospectively the patients who were received adriamycin and doxorubicin (AD) and adriamycin, cyclophosphamide and paclitaxel (ACT) as neoadjuvant chemotherapy and then received operation from 1 January, 2006 to 30 September, 2011. The group of AD regimen were scheduled for either 3 cycles of AD (50 mg/m<sup>2</sup> and 75 mg/m<sup>2</sup>, respectively), complete resection, and then 3 cycles of AD,