429 Poster

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

J. Horiguchi[1], D. Takata[1], N. Rokutanda[1], R. Nagaoka[1], A. Sato[1], H. Tokiniwa[1], K. Tozuka[1], M. Kikuchi[1], Y. Iino[2], I. Takeyoshi[1]. [1]*Gunma University Graduate School of Medicine, Maebashi Gunma, Japan;* [2]*Kusunoki Hospital, Fujioka Gunma, Japan*

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.

M. Zarchin[1], S. Paluch-Shimon[2], B. Kauffman[2], E.L. Shabtai[3], M. Gutman[4], M. Papa[4], T. Modiano[5], M. Shabtai[5]. [1]*Sheba Medical Center, Surgery, Ramat Gam, Israel;* [2]*Sheba Medical Center, Oncology, Ramat Gam, Israel;* [3]*Tel Aviv University TASMC, Statistics, Tel Aviv, Israel;* [4]*Sheba Medical Center, Surgery, Ramat Gan, Israel;* [5]*Sheba Medical Center, Oncology, Ramat Gan, Israel*

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 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 ilymph 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 raditherapy. 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

T. Iwase[1], R. Nakamura[1], M. Itami[2], T. Miyaki[1], T. Okada[1], Y. Onai[1], N. Yamamoto[1], M. Miyazaki[3]. [1]*Chiba Cancer Center, Breast Surgery, Chiba, Japan;* [2]*Chiba Cancer Center, Clinical Pathology, Chiba, Japan;* [3]*Chiba Graduate School of Medicine, General Surgery, Chiba, Japan*

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, axillar lymph node metastasis, and applying taxanes in neo-adjuvant chemotherapy did not showed 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 Doxetaxel and Adriamycin, Cyclophosphamide and Paclitaxel in Patients with Locally Advanced Breast Cancer Receiving Neoadjuvant Chemotherapy

W. Hong[1], K. Kim[1], Y. Jung[1], J. Kim[1], S. Kang[2], J. Chun[2], M. Chun[3], H. Yim[3], D. Kang[4], T. Kim[4]. [1]*Ajou University School of Medicine, Department of Surgery, Suwon, Korea;* [2]*Ajou University School of Medicine, Department of Hematology-Oncology, Suwon, Korea;* [3]*Ajou University School of Medicine, Department of Radiation Oncology, Suwon, Korea;* [4]*Ajou University School of Medicine, Department of Diagnostic Radiology, Suwon, Korea*

Background: It is well known that neoadjuvnat 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 adriamycine and doxetaxel(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 ether 3 cycles of AD(50 mg/m^2 and 75 mg/m^2, respectively), complete resection, and then 3 cycles of AD,

consevutively or 6 cycles of AD and then complete resection. Each cycle of chemotherapy in this group was performed at the interval of 3 weeks. The group of ACT was scheduled for 4 cycles of AC regimen (50 mg/m^2 and 500 mg/m^2, respectively) and then 4 cycles of paclitaxel(175 mg/m^2) at the interval of 3 week, respectively, before surgery. The patients who were confirmed systemic metastasis at the time of initial diagnosis or within 3 month after surgery and received therapy other than routine scheduled regimen were excluded.

Results: The patients who were enrolled in this study were totally 78 (AD and ACT were identically 38.) The significant differences of patients' characteristics before neoadjuvant chemotherapy were not observed between two groups. However, the significant differences were identified in hematologic toxicity including neutropenia more than grade 3 ($p < 0.001$), neutropenic fever ($p < 0.001$), dose reduction due to hematologic toxicity ($p = 0.012$) and chemotherapy induced anemia ($p = 0.012$), although chemotherapy induced thrombocytopenia ($p = 1.0$) was not different between two gruops. No differences were identified in non-hematologic toxicity including hepatic toxicity [AST ($p = 1.0$), ALT ($P = 0.783$) and bilirubin($p = 1.0$)], gastrointestinal toxicity [nausea, vomiting ($p = 0.529$) and diarrhea ($p = 1.0$)[and peripheral neuropathy ($p = 1.0$). The response of chemotherapy was no difference between two group, which was estimated by conversion rate of breast conserving surgery ($p = 1.0$), clinical response of chemotherapy ($p = 0.148$), clinically downstaging rate ($p = 0.464$) and pathologic complete response rate ($p = 1.0$). There is no factor to predicting pathologic complete response or conversion to breast conservation in this study.

Conclusions: The ACT regimen, compared to AD regimen, has an equivalent response to chemotherapy and a less side effect.

433 Poster

Recurrence Score (RS) and Treatment Decisions in Node-positive (N+), Estrogen Receptor-positive (ER+) Breast Cancer Patients in Israel

S.M. Stemmer[1], N. Lieberman[2], N. Efrat[3], D.B. Geffen[4], M. Steiner[5], L. Soussan-Gutman[6], S. Merling[2], S. Rizel[1], S.H. Klang[2]. *[1]Davidoff Center Rabin Medical Center Sackler Faculty of Medicine, Institute of Oncology, Petah Tikva, Israel; [2]Clalit Health Services, Community Division, Tel Aviv, Israel; [3]Kaplan Medical Center, Dept of Oncology, Rehovot, Israel; [4]Soroka University Medical Center and Ben-Gurion University of the Negev, Dept of Oncology, Be'er Sheva, Israel; [5]Carmel Hospital/Lin Medical Center, Oncology Service, Haifa, Israel; [6]Teva Pharmaceutical Industries Ltd, Netanya, Israel*

Background: RS, determined using the Onco*type* DX® assay, has a prognostic utility and can predict response to chemotherapy in node negative ER+ breast cancer patients. We evaluated the relationship between RS and treatment decisions in N+/ER+ breast cancer patients in Israel.

Materials and Methods: Eligible patients had micrometastases (Nmic) or 1−3 positive nodes, ER+ breast cancer and were reimbursed by Clalit Health Services (CHS) for the Onco*type* DX assay between 3/2006 and 11/2009. Claims data were reviewed to identify treatment received (chemotherapy plus hormonal therapy [CHT] vs hormonal therapy alone [HT]).

Table: Proportion of CHT-treated patients by RS, nodal status, and age group

Age group	Low RS (<18)	Intermediate RS (18−30)	High RS (⩾31)
Nmic			
<40 y (n = 3)	0% (0/1)	− (0/0)	100% (2/2)
40−55 y (n = 51)	3.6% (1/28)	26.3% (5/19)	100% (4/4)
>55 y (n = 81)	4.1% (2/49)	28.0% (7/25)	100% (7/7)
Total (n = 35)	3.8% (3/78)	27.3% (12/44)	100% (13/13)
1 positive node			
<40 y (n = 2)	0% (0/1)	100% (1/1)	− (0/0)
40−55 y (n = 27)	26.7% (4/15)	63.6% (7/11)	100% (1/1)
>55 y (n = 72)	7.1% (3/42)	35.7% (10/28)	100% (2/2)
Total (n = 101)	12.1% (7/58)	45% (18/40)	100% (3/3)
2−3 positive nodes			
<40 y (n = 1)	− (0/0)	0% (0/1)	− (0/0)
40−55 y (n = 10)	0% (0/6)	50% (2/4)	− (0/0)
>55 y (n = 35)	7.1% (1/14)	42.1% (8/19)	100% (2/2)
Total (n = 46)	5.0% (1/20)	41.7% (10/24)	100% (2/2)
All patients			
N = 282	7.1% (11/156)	37.0% (40/108)	100% (18/18)

Results: 282 patients were included in the analysis (6 patients <40 y; 88 patients between 40 and 55 y; 188 patients >55 y). Distribution of nodal status and age as well as RS results are shown in the Table. In total, after having the RS, 69 patients (24%) received CHT and 213 patients (76%) received HT. Overall, 7% of patients with low RS, 37% of patients with intermediate RS, and 100% of patients with high RS received CHT. In all examined nodal status groups, the proportion of CHT-treated patients was smaller in the low RS group than in the corresponding intermediate RS group and all patients with high RS received CHT (Table).

Conclusions: The RS seems to impact treatment decisions in N+ (Nmic or 1−3 positive nodes) ER+ breast cancer patients over 55 y in Israel more than nodal status. In younger patients data are limited due to a small sample size.

434 Poster

Phase II Study of Neoadjuvant Pegylated Liposomal Doxorubicin and Cyclophosphamide +/− Trastuzumab Followed by Docetaxel in Locally Advanced Breast Cancer (LABC)

M.K. Tuxen[1], S. Cold[2], U.B. Tange[3], S.B. Soendergaard[4], D.L. Nielsen[1]. *[1]Herlev University Hospital, Dept. of Oncology, Herlev, Denmark; [2]Odense University Hospital, Dept. of Oncology, Odense, Denmark; [3]Rigshospitalet, Dept. of Oncology, Copenhagen, Denmark; [4]Herlev University Hospital, Dept. of Nuclear Medicine, Herlev, Denmark*

Background: The primary end point of this study was the clinical response rate of neoadjuvant pegylated liposomal doxorubicin (Caelyx®) and cyclophosphamide +/− trastuzumab followed by docetaxel in patients with LABC. Secondary end points included determination of the rate of pathological complete response (pCR) and evaluation of the safety of the combination regimen.

Material and Methods: Patients (pts) with inflammatory, locally advanced breast cancer or a tumor >5 cm were enrolled. Pts received 4 cycles of pegylated liposomal doxorubicin 35 mg/m^2 and cyclophosphamide 600 mg/m^2 on q21d followed by 4 cycles docetaxel 100 mg/m^2 q21d. Pts with HER2-positive tumors were concurrently treated with trastuzumab 6 mg/kg q21d for 8 cycles.

Results: From March 2009 to October 2010 49 pts were enrolled. One pt was excluded from the study as she turned out to have sarcoma. Thus, 48 pts were assessable for toxicity. The median age was 50 years (range 31−69). 26 pts. (54%) were premenopausal and 22 (46%) postmenopausal. 14 pts (29%) had tumor T4, 32 (67%) T3 and 2 (4%) T2. 11 pts (23%) had HER2-positive tumor and 7 (15%) had triple negative tumor.

All 8 cycles of neoadjuvant therapy were completed as planned in 40 pts (83%), 6 (13%) discontinued treatment due to toxicity after 5−7 cycles and 2 pts discontinued due to clinical suspicion of progression and patient's wish, respectively. One patient developed an anaphylactic reaction to the first infusion of pegylated liposomal doxorubicin. 47 pts were therefore assessable for response evaluation.

Investigator-assessed clinical response rate was 83%, 3 pts (6%) had a clinical complete response and 36 (77%) had a partial response. One patient was clinically suspected for progression but operation showed response. pCR rate was 19% (9 pts).

The primary toxicity observed was skin toxicity. Palmar-plantar erythrodysesthesia (PPE) grade 3 was observed in 10 pts (21%) and grade 4 in 6 (13%). Other most frequent grade ⩾3 adverse events were: pain (31%), neurotoxicity (21%), fatigue (21%), febrile neutropenia (19%), mucositis (8%). No changes in cardiac function were seen. There were no treatment-related deaths.

Conclusions: The combination of pegylated liposomal doxorubicin and cyclophosphamide +/− trastuzumab followed by docetaxel is highly active in LABC with an acceptable safety profile. The primary toxicity was cutaneous toxicity which was manageable.

435 Poster

Genetic Variability in the Methylenetetrahydrofolate Reductase (NAD(P)H) Gene (MTHFR) is Associated with Severe Non Hematological Toxicity of Adjuvant FEC in Breast Cancer

C. Vulsteke[2], D. Lambrechts[1], A.S. Dieudonné[3], S. Hatse[4], B. Brouwers[2], T. Van Brussel[1], P. Neven[5], A. Belmans[6], R. Paridaens[2], H. Wildiers[2]. *[1]Catholic University of Leuven, Vesalius Research Center, Leuven, Belgium; [2]University Hospitals Leuven, General Medical Oncology, Leuven, Belgium; [3]Catholic University of Leuven, Multidisciplinary Breast Center, Leuven, Belgium; [4]Catholic University of Leuven, Experimental Oncology, Leuven, Belgium; [5]University Hospitals Leuven, Multidisciplinary Breast Center, Leuven, Belgium; [6]Catholic University of Leuven, Leuven Biostatistical Center, Leuven, Belgium*

Background: We assessed the impact on non hematological chemotherapy toxicity of single nucleotide polymorphisms (SNP) in germline DNA in a panel of potential genes of interest through high throughput sequencing. First aim was to validate the predictive value of certain SNP