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Updated results of the assessment of the role of her-2 overexpression as a predictive factor to neoadjuvant, anthracycline-containing chemotherapy in locally-advanced breast cancer (LABC)

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Objective: to assess, whether HER-2 overexpression has any influence to response to neoadjuvant chemotherapy, containing anthracyclines. Secondary endpoint was association of HER-2 positivity with time to progression (TTP) and overall survival (OS) after neoadjuvant treatment of LABC.

Methods: ninety-six consecutive patients (pts) with LABC were treated with anthracycline-containing neoadjuvant chemotherapy and underwent radical surgery between 12.2002 and 12.2003.HER-2 expression was determined by routine clinical laboratory assesment. Tumors with 3+ immunohistochemistry staining intensity or gene amplification by fluorescent in situ hybridization were considered HER-2 positive. Patients were divided into 2 groups according to HER-2 expression: I – negative: N = 50; II-positive: N = 46.Response to neoadjuvant chemotherapy was assesed by physical, pathologic and imaging examination; TTP and OS by Kaplan-Meier analysis.

Results: forty-six (47%) pts had HER-2 positive tumors. Median age was: I – 52 (35–74), II – 53 (35–76) yrs. ⩾T2 tumors: I – 34 (68%), II – 33 (72%) pts. Most common chemotherapy was AC regimen: I – 36 (72%), II – 34 (74%) pts; doxorubicin + docetaxel (AT) received: I – 7 (14%), II – 3 (7%); other, such as FAC, FEC, T/ET or doxorubicin monotherapy were rare: I – 7 (14%), II – 9 (19%) pts altogether. At least 4 cycles of chemotherapy received: I – 48 (96%), II – 43 (93%) pts. The clinical response rate (complete response [CR] and partial response [PR]) was: I – 58% (29/50), II – 72% (33/46), CR I – 16% (8/50), II – 17% (8/46) pts. Pathological CR was achieved in: I – 6% (3/50), II – 6.5% (3/46) pts. Median time of follow-up was 23 months. Twenty-seven relapses were noted: I – 12 (24%), II – 15 (33%). Median TTP was I – 22 months, II – 16 months. Time for OS has not been reached yet.

Conclusion: there was a tendency to better response for HER-2 positive tumors. We found no significant correlation between TTP and HER-2 overexpression. More patients and longer follow-up is needed to draw further conclusions, but better response and more relapses in HER-2 positive group suggest that anthracycline-containing chemotherapy followed by trastuzumab may be a better therapeutic option for these patients. The analysis of further cases included to analysis since 01.2004 and results of follow-up of remaining patients will be presented.

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Relative dose intensity (RDI) relevance in adjuvant CMF chemotherapy of breast cancer

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Background: Intensity of adjuvant chemotherapy in breast cancer patients is considered a prognostic factor, although published results are conflicting. In this study we retrospectively analyzed the impact of RDI in early breast cancer patients administered adjuvant CMF.

Material and Methods: Between 1990 and 1997 a total of 285 consecutive breast cancer patients received adjuvant CMF chemotherapy (100 mg/m^2 cyclophosphamide p.o. on days 1–14, 40 mg/m^2 i.v. methotrexate on days 1 and 8, and 600 mg/m^2 i.v. 5-fluorouracil on days 1 and 8, q. 4 weeks, for a total of six cycles). Twenty patients were excluded from the analysis due to inadequate number of cycles actually administered (⩽4). Postoperative radiotherapy and endocrine therapy was applied in 16% and 10% of patients, respectively. Median age was 46 years (range, 30–62 years), 66% of patients had nodal involvement, 82% of tumors were ductal carcinomas, and 40% were grade 3. The administered dose intensity of cyclophosphamide, methotrexate and 5-fluorouracil relative to the planned dose intensity was calculated for each patient. Univariate and multivariate survival analysis was performed with log rank test and Cox proportional hazards model with the use of Wald's statistics to test each variable in backward-stepwise regression. RDI was categorized only after the final model had been found.

Results: Median follow-up was 7.7 years (range 4.0–11.6 years). Actuarial survival probability at 5 and 10 years was 76% and 62%, respectively. The number of involved axillary lymph nodes was the strongest predictor of outcome. Median RDI for cyclophosphamide, methotrexate and 5-fluorouracil was 83%, 77% and 93%, respectively. Median average dose intensity for all drugs was 86%. RDI of 78% and more was significant predictor of overall survival, with 0.6 hazard risk of death (95% CI 0.37–0.99; p = 0.045) and 0.57 hazard risk of relapse (95% CI 0.35–0.92; p < 0.001).

Conclusions: RDI is a strong and independent predictor of overall survival and disease-free survival in breast cancer patients administered adjuvant CMF chemotherapy, with 78% being the best cut-off discriminating value.

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Pathological response to preoperative concurrent chemoradiotherapy for breast cancers considered too large for initial conserving surgery: results of a phase II study

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Introduction: This study aimed to evaluate the rate of pathological complete response to preoperative chemoradiotherapy and its level of acute toxicity.

Material and Methods: Sixty women were treated (11/2001–11/2003) by preoperative chemoradiotherapy and breast surgery. One patient withdrew her consent during treatment. Median age was 49 years (31–65). Median maximal diameter was 45 mm (21–80). Clinical axillary stages consisted of 54% N0 and 46% N1. Some tumours presented with pathological features of aggressiveness (25% histological grade 3, 27% absence of hormonal receptors, 14% HER2 over-expressed). Chemotherapy consisted of 4 cycles of 5FU 500 mg/m^2 (day 1 – day 5) and Vinorelbine 25 mg/m^2 (day1; day 6). Starting with the second cycle, radiotherapy delivered 50 Gy to the breast and 46 Gy to the internal mammary and supra/infraclavicular lymph nodes. Breast surgery (mastectomy or lumpectomy) and axillary lymph node dissection were then performed. Pathological complete response was defined as less than 5% of residual invasive epithelial cells in the tumour, without any mitosis.

Results: The rate of pathological complete response (pCR) was 27% (16/59). Three factors were associated with pCR: histological grade 3, absence of hormonal receptors and a number of mitoses above 10 per 10 high power fields. Breast-conservation was possible in 69% of patients (41/59). Four patients (7%) had to stop their chemotherapy because of toxicity. No patient had diminished radiotherapy dose because of toxicity. There was no toxic death. Twenty-one patients (36%) experienced a grade 3 toxicity and 13 (22%) a grade 4. The only grade 4 toxicities were haematological (22%) or gastrointestinal (2%).

Conclusion: Chemoradiotherapy showed good efficacy, both in terms of pathological complete response (27%) and in allowing breast conservation (69%) with acceptable tolerance. Long-term follow-up is needed to confirm that these good pathological results bode well in terms of patients' outcome.

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Multicenter phase II trial of neoadjuvant exemestane for postmenopausal patients with hormone-sensitive, operable breast cancer: Saitama Breast Cancer Clinical Study Group (SBCCSG-03)

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Back ground: Randomized trials have shown that neoadjuvant letrozole and anastrozole can reduce tumor volume, allowing breast-conserving surgery (BCS) rather than mastectomy for operable tumors. Type I anti-aromatase agent exemestane (EXE) is also promising, however; its use for neoadjuvant therapy has not been reported.

Purpose: Multicenter phase II trial (SBCCSG-03) was designed to evaluate the efficacy and tolerability of neoadjuvant EXE for postmenopausal patients (pts) with estrogen receptor (ER) and/or progesterone receptor (PR) positive breast cancer.

Patients and Methods: Postmenopausal pts with ER and/or PR positive, stage II to IIIB and 3 cm or larger-sized operable breast cancer were assigned to neoadjuvant EXE (25 mg daily) for 4 months and followed by surgery. The pathological response defined as grade 1b, 2 or 3 was assessed by a central review according to "General Rules for Clinical and Pathological Recording of Breast Cancer 2005" published by The Japanese