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Retrospective analysis of cardiac safety in EBC women treated with the chemotherapy regimen: FEC followed by docetaxel+trastuzumab

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Background: Around 25% of the patients suffering from early breast cancer express the Her-2 receptor. Trastuzumab has shown to improve survival, especially when given in the adjuvant setting. Trastuzumab has also strong synergy with Docetaxel in metastatic breast cancer. For these reasons, clinicians in Belgium often prescribe Docetaxel associated with concomitant Trastuzumab in the adjuvant setting. Docetaxel is itself often given after FEC100, as in the PACS01 trial. Today, there is not any data supporting this treatment scheme and especially no cardiac safety data. This latest point is our major concern since these treatments are intended to cure the patients. Significant decrease of the left ventricular ejection fraction (LVEF) with adjuvant Trastuzumab has been reported to occur in 0.5% to 4% of treated patients.

Methods: We retrospectively reviewed 37 patients with early-stage HER2-positive breast cancer who were treated with curative surgery and chemotherapy in two centers. We evaluated the cardiac safety of this treatment regimen. We have recorded for each patient the type of treatment received, the cardio-vascular risk factors and LVEF calculated by two methods (MUGA or echo) and assessed at baseline, and then every 3 months. Decline of LVEF was defined as a 10% drop or an absolute value <50%.

Results: The median age of the patients was 53 years. The treatment consisted in 3−4 cycles of FEC100 followed by 3−4 cycles of Docetaxel (100 mg/m^2) and Trastuzumab concurrently. Trastuzumab was administrated during one year without interruption for 34 patients (92%). One patient stopped definitively after ten months and two patients discontinued for 1 and 2 months respectively due to asymptomatic decrease of their cardiac function (<10%). In this small retrospective analysis, we reported that 7.7% of the patients presented with an asymptomatic decline of their LVEF. However the median follow-up time was only 16 months, which could underevaluate this problem. Disease-free and overall survivals were not computed due to the low number of patients included in this retrospective analysis.

Conclusion: When Trastuzumab is given with Docetaxel 100 mg/m^2 just after the Anthracyclin-based chemotherapy, the incidence of cardiac event seems to be higher than previously reported. To confirm these data a longer follow-up is needed as well as a larger prospective trial using this scheme of adjuvant treatment.

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Neoadjuvant trastuzumab therapy with or without anthracycline containing chemotherapy for HER2-positive primary breast cancer

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Background: Trastuzumab and chemotherapy combinations have already shown superior results in metastatic breast cancer patients. The purpose of this study is to determine the clinical and pathological efficacy of neoadjuvant chemotherapy (NAC) using trastuzumab and chemotherapy with or without anthracyclines for primary breast cancer patients with HER2-positive tumors.

Patients and Methods: A retrospective analysis of 32 primary breast cancer patients (IIA-IIIC) with HER2-positive tumors treated by NAC was performed. NAC consisted of weekly paclitaxel plus trastuzumab with (PTA group, n = 12) or without anthracycline (PT group, n = 20). Patients in the PTA group received 4 courses of FEC every 3 week followed by concomitant paclitaxel 80 mg/m^2 and trastuzumab weekly for 12 weeks and those in the PT group received 4 courses of paclitaxel 80 mg/m^2 weekly (Days 1, 8, 15) followed by a 1-week break and trastuzumab weekly.

Results: Median age of patients was 49 years old. Of 32 patients, 15 (47%) had a pathologic complete response (pCR). Patients with clinical stage II breast cancer achieved a significantly higher pCR rate than those with clinical stage III breast cancer. There was no significant difference in age, clinical stage and clinical response rate between the PTA and the PT groups. The pCR rate of the PTA and the PT groups was 42% and 50%, respectively. At the median follow up of 28 months, there was no significant difference of disease-free survival between the two groups.

Conclusion: Trastuzumab-containing NAC is effective irrespective of anthracyclines in the treatment of primary breast cancer patients with HER2-positive tumors.

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Long-term follow-up of node negative grade 3 early breast cancer patients − single center experience

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Background: Among all node negative early breast cancer (BC) patients, tumor grade 3 represents a poor prognostic factor and adjuvant systemic therapy is usually given to these patients. We reported disease outcome in these women after prolonged follow-up.

Patients and Methods: A group of tumor grade 3 node negative BC patients that underwent radical surgery from 1984 to 1994 was separated. According to the Protocol for the malignant diseases management at that time, the only node-negative patients who were given adjuvant systemic therapy were patients with grade 3 BCs (medullar BCs were excluded): adjuvant endocrine therapy was given to patients with SR+ BC, while adjuvant chemotherapy consisting of cyclophosphamide–methotrexate−5FU (CMF) regimen was given to SR− BC patients. Steroid receptors contents were determined by the classical biochemical DCC method.

Results: One hundred and thirty five patients (56 premenopausal and 79 postmenopausal) median age of 57.9 years (range 38−76) were analyzed. Predominant tumor histology was invasive ductal carcinoma (68%) with pT2 tumor size in 71% of patients. SR status was unknown for 32/135 (24%) patients, 52/135 (38%) patients had SR+ and 51/135 (38%) patients had SR− BC. After median follow-up of 12 years, mean disease-free interval (DFI) was 134 months (95% CI 118–149) and overall survival (OS) 147 months (95% CI 132–162). Whole group was divided into 4 subgroups in relation to which adjuvant systemic therapy was given: no therapy subgroup (N = 25), adjuvant ovarian ablation by irradiation (N = 15, all premenopausal), adjuvant Tamoxifen (N = 29, all postmenopausal) and adjuvant CMF chemotherapy (N = 66). ER and PgR contents were significantly lower in patients who received adjuvant CMF chemotherapy in comparison with patients who were treated either with adjuvant Tamoxifen ($p < 0.0083$ for both SRs) or adjuvant ovarian ablation ($p < 0.0083$ for both SRs). There was no difference in either DFI or OS between patients treated with adjuvant Tamoxifen and patients without adjuvant therapy and between patients treated with adjuvant CMF chemotherapy and patients treated with ovarian ablation, as well. However, patients who received adjuvant CMF therapy had significantly longer both DFI (Long rank test, $p = 0.0016$) and OS (Long rank test, $p = 0.009$) compared to patients without therapy. Similarly, DFI (Long rank test, $p = 0.01$) and OS (Long rank test, $p = 0.001$) in women treated with ovarian ablation were significantly prolonged compared to subgroup without adjuvant therapy.

Conclusion: Our long-term follow-up data confirm that node negative grade 3 untreated BC patients had worse disease outcome compared to patients treated with adjuvant CMF chemotherapy and ovarian ablation. Surprisingly, patients treated with adjuvant Tamoxifen had no better disease outcome as compared with untreated women, which, in the first place, might be attributable to shorter course of adjuvant therapy.

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Bone metabolism and quality of life of postmenopausal women with invasive breast cancer receiving neoadjuvant hormonal therapy: sub-analyses from celecoxib anti-aromatase neoadjuvant (CAAN) trial

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Background: Anti-aromatase therapy is important in the treatment of breast cancer in postmenopausal women, but assessments on bone metabolism and Quality-of-life (QoL) are seldom performed in studies of neoadjuvant hormonal therapy (NHT) for breast cancer (BC). In this substudy, changes in bone metabolism and QoL during NHT were presented here.

Patients and Methods: 82 postmenopausal patients with invasive hormone-sensitive BC were randomized to receiving exemestane 25 mg QD and celecoxib 400 mg BID (group A, n = 30), exemestane 25 mg QD (group B, n = 24) and letrozole 2.5 mg QD (group C, n = 28). Bone mineral density (BMD) of 48 patients (Group A, n = 23; Group B, n = 10; Group C, n = 15) was analyzed. The serum bone-specific alkaline phosphatase (bap)