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Anthracycline and concurrent radiotherapy significantly reduced loco-regional breast cancer relapse rate

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Background: The optimal sequencing of chemotherapy and radiotherapy after breast surgery was largely studied but remains controversial. Concurrent chemo-radiotherapy is a valuable method for adjuvant treatment of breast cancer which is under continuous ongoing research program in our hospital. We are evaluating the efficacy and feasibility of the concomitant use of anthracycline with radiotherapy, retrospectively.

Materials and Methods: Four hundred women having breast cancer were investigated in a retrospective study. All patients were either treated by radical surgery or breast conservative surgery. The study compares two adjuvant treatments associating concomitant chemotherapy and radiotherapy. In a first group (group A) the patients were treated by chemotherapy and radiotherapy in concomitant way using anthracycline. In a second group (group B) the patients were treated by chemotherapy and radiotherapy in concomitant way using CMF treatment. Chemotherapy was administered in six cycles, one each 3 weeks. Radiotherapy delivered a radiation dose of 50 Gy on the whole breast (or on the external wall) and/or on the lymphatic region. This study is the follow up of a previous investigation which concerned 244 patients selected within a 2 years period (Ismaili et al. Concurrent chemoradiotherapy in adjuvant treatment of breast cancer. *Radiation Oncology* 2009, **4:**12). In our ongoing work we are confirming our finding about our previous.

Results: after 76.4 months median follow-up, only one patient relapsed to loco-regional breast cancer when the treatment was based on anthracycline. However, 8 patients relapsed to loco-regional breast cancer when the treatment was based on CMF. In the anthracycline group, the disease free survival after 5 years, was 80.4% compared to 76.4% in the CMF group (Log-rank test: p = 0.136). The overall survival after 5 years was 82.5% and 81.1% in the anthracycline and CMF groups respectively (Log-rank test: p = 0.428). The loco-regional free survival at 5 years was equal to 98.6% in group A and 94% in group B (Log-rank test: p = 0.033). The rate of grade II and grade III anaemia was 13.9% and 6.7% in anthracycline group and CMF group respectively (Khi^2-test: p = 0.009). The rate of grade II and grade III skin dermatitis toxicity was 4.5% in the group A and 0% in the group B (Khi^2-test: p = 0.013).

Conclusion: From our ongoing investigations we showed and confirmed that the treatment based on anthracycline and concurrent radiotherapy significantly reduced loco-regional breast cancer relapse rate.

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Incidence of brain metastases in early stage high risk Her2 3+ breast cancer patients

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Background: Correlation between HER2 3+ and brain metastases is quite convincing in metastatic breast cancer (BC), hence 25−46% of these patients, develops brain metastases (BM) eventually. This predisposition of Her2 3+ BC to disseminate in the brain is confirmed also in adjuvant trastuzumab trials.

The objective of this analysis is to prospectively explore the incidence and timing of development of BM in high risk Her2 3+ BC patients.

Material and Methods: Among 758 patients treated with chemotherapy for early BC, (January 2007–October 2009) In this analysis, we have included only 258 Her2 3+ pts. that had sufficient follow up time (median 18 months). All patients had usual initial diagnostic procedures according to the disease stage. Brain CT was performed only if CNS symptoms developed but also, patients have been offered brain CT in absence of CNS symptoms during adjuvant trastuzumab as a part of initial diagnostic procedures.

Results: Eighty eight patients (34%) consented and underwent brain CT in the absence of CNS symptoms. Median number of trastuzumab cycles at the time of brain CT was 9 (4−18) There were no occult CNS metastases detected by brain CT in 88 asymptomatic patients, During adjuvant treatment, 2 pts (0.77%) developed symptomatic CNS metastases, synchronously with other metastases sites. During a median follow up of 18 months 5/258 (1.93%) patients developed brain metastases eventually, 2 while receiving adjuvant trastuzumab (Table 1). Median time from breast cancer diagnosis to brain metastases development was 32 months (range 14−43). Relapses to any other organ site were registered in 15 pts (5.8%). Two patients had solitary BM that were removed, and Her2 3+ was also confirmed in brain metastases.

Table 1: Characteristics of patients with BM

Pt	Age at BC diagnosis	Histology/ grade	N status	ER score	PGR score	Brain CT before	DFI (months) to	
						brain meta	BM	Other metastases
1	35	Medullar/ grade 2	10/20	2	3	No	14	14
2	37	Ductal/ grade 3	13/18	5	3	No	24	12
3	41	Ductal/ grade 2	2/17	2	0	Yes	41	No other metastases
4	47	Ductal/ grade 2	15/15	5	0	Yes	43	22
5	54	Mucinous/ grade 3	6/15	0	0	No	18	No other metastases

Conclusion: The overall incidence of BM was 1.93%, during a median follow up of 18 months. We could not prove that brain CT in asymptomatic stage is of any value in this high risk group of patients. All patients would be prospectively followed up for a definitive disease outcome.

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The addition of capecitabine to neoadjuvant chemotherapy for early breast cancer (EBC): a review of clinical study data

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Background: Neoadjuvant chemotherapy (CTX) is standard care for locally advanced, stage III invasive, and some stage II breast cancers, but no regimen has emerged as a clear leader.

Methods: To determine the impact of the integration of capecitabine (C) into neoadjuvant anthracycline/taxane-based CTX for EBC, randomised, phase III studies and a large phase II study evaluating C in neoadjuvant anthracycline/taxane-based CTX regimens for EBC were analysed in a fixed-effects meta-analysis. Data are also available from a GBG/AGO Intergroup phase III study of C as neoadjuvant CTX. However, these were not included in the meta-analysis due to the high proportion of patients (>30%) receiving trastuzumab in this study. The primary endpoint of the studies was pathological complete response (pCR) rate. The definition of pCR included ductal carcinoma in situ in the breast.

Results: See the table.

	ABCSG-24 phase III trial n = 512, 2-arm	Korean phase III trial n = 209, 2-arm	French phase II trial n = 182, 2-arm
CTX	EDC vs ED	DC vs ACyc	CycEC vs CycEF
pCR rate	24.3% vs 16.0%	21% vs 10%	20% vs 13%
p-value	0.02	0.024	Noninferiority

In the ABCSG-24 trial, patients with operable breast cancer received 6× epirubicin/docetaxel q3w (E 75 mg/m^2 and D 75 mg/m^2 day 1; pegfilgrastim 6 mg day 2) ± C 1,000 mg/m^2 b.i.d. days 1−14. In the Korean trial, patients with node-positive EBC received 4 x 3-weekly cycles of DC (D 75 mg/m^2 day 1; C 1,000 mg/m^2 b.i.d. days 1−14) or doxorubicin/cyclophosphamide (A 60 mg/m^2, Cyc 600 mg/m^2 day 1). In the French phase II trial, patients with EBC received 4 × 3-weekly cycles of CycEC (Cyc 500 mg/m^2, E 100 mg/m^2 day 1, plus C 1,000 mg/m^2 b.i.d. days 1−14) or 5-fluorouracil (F) plus ECyc (F 500 mg/m^2, E 100 mg/m^2, Cyc 500 mg/m^2 day 1). The integration of C into neoadjuvant CTX showed a significantly increased pCR rate according to a fixed-effects meta-analysis (relative risk 1.62; 95% CI 1.21−2.16; I^2 = 0.0%, n = 3).

Conclusions: These data support the integration of C into neoadjuvant anthracycline and/or taxane-based CTX regimens.