

metastases was brain in 17.8% of relapsing patients (35% of relapsing patients who received T). The 2 year RFS among patients receiving concurrent chemotherapy + T was 94.7% whereas sequential CT followed by T was 98.4%. In the T treated cohort the 2 year RFS among node negative and node positive patients were 97.8% and 94.4% respectively ($p = 0.06$). In the cohort of HER-2 positive patients who did not receive T, the 2 year RFS among node negative and node positive patients were 90.7% and 75.5% respectively ($p = 0.007$). The corresponding 2 year distant RFS in this same cohort was 93.1% and 80.3% respectively ($p = 0.01$).

Conclusions: A population based analysis of adjuvant trastuzumab use among Canadian women demonstrates highly favorable outcomes at the 2 year follow-up period. Although retrospective in nature, this is one of the first studies to observe breast cancer outcomes in a more generalized population with widespread publicly funded use of T.

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Poster discussion

Independent prognostic factors for response: updated results of the ABCSG-24 study evaluating the addition of capecitabine to epirubicin-docetaxel neoadjuvant therapy for early breast cancer (EBC)

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Background: The randomised, phase III ABCSG-24 study evaluated the influence of the addition of capecitabine (C) to 6 cycles of neoadjuvant epirubicin-docetaxel (ED; EDC therapy) on pathological complete response (pCR) rate in patients with EBC. Additional objectives were comparison of the rates of breast conservation (BCR) and axillary lymph node involvement at the time of final surgery. The aim of the current analysis was to assess the role of known risk factors on response to EDC.

Methods: Patients with biopsy proven, operable breast cancer (except T4d), +/- nodal involvement, who were scheduled for neoadjuvant chemotherapy were stratified according to known risk factors (menopausal status, hormone receptor status, tumour grade and stage, HER2 status) and randomised to 6 x ED every 21 days (day 1: E 75 mg/m² i.v., D 75 mg/m² i.v., day 2: pegfilgrastim 6 mg) +/- C (2 x 1,000 mg/m²/day for 14 days). The accrual target was 536 patients (94 with HER2-positive disease) to achieve 510 evaluable patients and detect a difference in the rate of pCR of 16% (ED) versus 27% (EDC) with a power of 83% at a significance level of 0.05 (two-sided Chi-squared test). Patients with HER2-positive disease were also randomised to neoadjuvant trastuzumab (T) or placebo.

Results: Baseline characteristics were well balanced between the ED (n=257) and EDC (n=255) groups. Median age was 49 years (range 25-73) and 67% and 74% of patients had hormone receptor-negative and HER2-negative tumours, respectively. pCR rate was significantly increased with EDC compared with ED (24.3% vs 16.0%; HR 0.58 [0.38-0.92], $p = 0.02$). A logistic regression model demonstrated that hormone receptor status ($p < 0.001$), tumour stage ($p = 0.002$) grade ($p < 0.001$), and C therapy ($p = 0.03$) were independent prognostic factors for pCR. Overall, no significant difference in BCR or rate of axillary lymph node involvement was noted. There was no significant difference in the incidence of serious adverse events (EDC 26% vs ED 21%) and 96% and 94% of patients receiving ED and EDC, respectively, completed all 6 cycles of therapy.

Conclusions: These data indicate that hormone receptor status, tumour stage and grade, and treatment with C are independent prognostic factors for response when C is integrated into a taxane-anthracycline-based neoadjuvant regimen.

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Poster discussion

Breast-conserving surgery after preoperative endocrine therapy versus chemotherapy in postmenopausal patients with estrogen-receptor-positive breast cancer

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Background: Neoadjuvant therapy may increase the proportion of women eligible for breast-conserving surgery (BCS) by reducing tumor size. Endocrine therapy and chemotherapy have been investigated in this setting.

Methods: A total of 239 patients (pts) with ER-positive and/or PgR-positive breast cancer (T2N1-2, T3N0-1, T4N0M0) were randomly assigned to receive neoadjuvant endocrine therapy (ET) [anastrozole 1 mg/day or exemestane 25 mg/day for 3 months, 121 patients] or chemotherapy (CT) [doxorubicin 60 mg/m² with paclitaxel 200 mg/m², four 3-week cycles, 118 patients]. All pts were considered to be ineligible for BCS at enrollment. After BCS all pts received radiotherapy (50 Gy in 25 fractions). The median follow-up time was 5.6 years.

Results: The primary efficacy end point was already reported (Cancer 2007; 110: 244-54). Overall response (OR=CR+PR) was similar in the ET group (65.5%) compared with CT (63.6%; $p > 0.5$).

After completing neoadjuvant treatment, 31 (13%) patients did not undergo surgery: 12.3% of pts who were receiving ET and 13.5% of pts who were receiving CT. Progressive disease was observed in 9% of pts who were receiving ET and 9% of pts who were receiving CT ($p > 0.5$). There was a trend toward higher overall rates of objective response (OR) and BCS among patients with tumors expressing high levels of ER (Allred score >6) in the ET group compared CT ($p = 0.054$; 43% vs 24% respectively). There was no significant difference between ET and CT relative to the incidence of locoregional recurrences and distant metastases (7.9% and 7.3%, $p = 0.99$; 14.8% and 15.2%, $p = 0.83$, respectively).

There was no significant difference in DFS through 5 years of follow up between the 121 pts who received neoadjuvant ET and 118 women who received CT: 71.0% and 67.7% ($p > 0.5$).

Fifty one (43%) pts who were receiving CT experienced neutropenia (grade 2-4) that led to treatment interruption. ET was well tolerated.

Conclusion: For elderly postmenopausal women with comorbid conditions and large hormone-responsive tumors (ER+ or PgR+) BCS may be possible after well-tolerated, preoperative ET with aromatase inhibitors less toxic than CT.

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Poster discussion

Homologous recombination deficiency in breast cancer and association with response to neo-adjuvant chemotherapy

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Background: Tumors with homologous recombination deficiency (HRD) are highly sensitive to DNA double strand break (DSBs) inducing agents, including alkylating agents and poly (ADP-ribose) polymerase (PARP)-inhibitors. BRCA1- and BRCA2- associated tumors, which are thought to be HRD, may be identifiable employing an array Comparative Genomic Hybridization (aCGH) classifier. As this classifier was primarily developed to recognize breast cancers in BRCA mutation carriers, we determined these profiles together with several other HRD characteristics in sporadic cancer patients and correlated the presence to neoadjuvant treatment response to DSB inducing chemotherapy.

Material and Methods: Forty-three triple negative (TN) and 91 estrogen receptor positive/HER2- (ER+/HER2-) pre-treatment biopsies were examined, procured from sporadic breast cancer patients scheduled to receive neoadjuvant therapy with doxorubicin/cyclophosphamide. aCGH for assessing BRCA1-like and BRCA2-like profiles was performed. In addition, BRCA1 promotor methylation, BRCA1 mRNA expression and amplification of the EMSY gene were assessed. Response to neoadjuvant treatment was assessed by measuring pathological complete remission (pCR) and near pCR at the time of surgery.

Results: Inactivation of BRCA1 was frequent in TN tumors: 54% of these tumors showed a 'BRCA1-like' profile at aCGH. BRCA1 promotor methylation and reduced BRCA1 mRNA expression were observed in 25% and 43% of the TN tumors, respectively. Although a slightly higher treatment response was seen in TN tumors with a BRCA1-like profile, this was not significant (70% vs. 42%, $p = 0.231$). In ER+ tumors, a BRCA2-like profile and the amplification of the BRCA2 inhibiting gene EMSY were frequently observed (37% and 15% respectively). A BRCA2-like profile was associated with a significantly higher response rate (35% vs 12%, $p = 0.033$). EMSY amplification and a BRCA2-like profile occurred together in only one case. EMSY was not associated with treatment response, questioning the role of EMSY in HRD.

Conclusion: Abnormalities associated with BRCA1 inactivation are present in about half of the TN breast cancers and may identify tumors that are sensitive to chemotherapy that causes DNA DSBs. In ER+/HER2- tumors, the BRCA2-like profile may indicate HRD and thus be predictive for benefit from new targeted agents, involved in DNA repair. After validation