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Safety and toxicity in Korean breast cancer patients receiving adjuvant TAC regimen chemotherapy – prospective multicenter clinical study

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Background and Purpose: More recently, a randomised phase III trial by the Breast Cancer International Research Group (BCIRG 001) has shown that the combination of docetaxel, doxorubicin, and cyclophosphamide (the TAC regimen) is superior to FAC as adjuvant chemotherapy for node-positive operable breast cancer. Unfortunately, TAC was clearly more toxic than FAC, not only with respect to neutropenic fever events, but also with respect to many extrahaematological side-effects. The aim of the study was to analyse the toxicity and tolerability of Korean breast cancer patients treated with TAC.

Materials and Methods: This study was carried out in 50 breast cancer patients who underwent primary surgery (i.e., modified radical mastectomy, skin sparing mastectomy, or breast conserving surgery) at the Department of Surgery in Soonchunhyang University (4 affiliated hospitals) from October of 2005 to March of 2007. They received a total of 260 courses consisting of TAC (75/50/500 mg/m^2 6$\times$q3wk). Toxicity was graded according to the National Cancer Institute Common Toxicity Criteria version 2.0.

Results: The main toxicities were hematologic (neutropenia grade 3/4 in 100% of patients and 95.6% of cycles; febrile neutropenia in 38% of patients and 15.9% of cycles). There was no cases of septic death. The peak time of occurrence of febrile neutropenia was 7−10 days after receiving chemotherapy (mean duration; 2.12 days). Severe nonhematologic adverse events were infrequent; myalgia (30%), fatigue (22%), stomatitis (20%), nausea (16%).

Conclusion: Adjuvant chemotherapy with TAC was tolerable in Korean breast cancer patients. Although neutropenia is frequent, its consequences are manageable. The rest of the toxicity profile seems acceptable, with no significant extrahematologic toxicities, including cardiac toxicity.

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Pegfilgrastim and darbepoetin alfa as haematopoietic support for adjuvant dose dense doxorubicin + cyclophosphamide–paclitaxel in early stage breast cancer patients – results from the ACCELERATE study

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Background: Delivery of full dose chemotherapy on schedule is critical to the success of dose dense (dd) chemotherapy regimens, and granulocyte colony-stimulating factor support is recommended in this setting. Furthermore, anaemia is a common side effect of dd chemotherapy. We evaluated the feasibility of delivering a 2-weekly anthracycline–taxane regimen to breast cancer patients (pts) with pegfilgrastim and darbepoetin alfa support.

Methods: This was an Australian, multicentre, open-label study in which women with early stage node-positive or high-risk node-negative breast cancer received adjuvant doxorubicin 60 mg/m^2 + cyclophosphamide 600 mg/m^2 every 2 weeks for 4 cycles, then four 2-weekly cycles of paclitaxel 175 mg/m^2 (ddAC $\rightarrow$ T). Pegfilgrastim 6 mg was given on Day 2 of each cycle and darbepoetin alfa was administered in cycles where pts' haemoglobin was <11 g/dL. The primary endpoint was the proportion of pts with chemotherapy dose delays ($\geqslant$7 days).

Results: Between 01/2006 and 07/2007, 83 pts were treated. Mean age ($\pm$SD, years) was 46.6$\pm$9.7, 90% had Stage II−III disease, and 80% were axillary lymph node positive. In total, 664 cycles were planned, of which 656 were delivered. Eleven pts had a dose delay $\geqslant$7 days (13 cycles delayed; 2 pts >1 cycle delayed), while dose reductions were less common (Table). Most dose delays resulted from non-haematological toxicity (mainly fever/infection, 3 patients). There were few grade 3−4 haematological toxicities; febrile neutropenia occurred in 4 pts (5%), 2 of whom required a dose reduction. Darbepoetin alfa was given to 54 pts (65%); only 1 pt (1%) received a red blood cell transfusion.

Endpoints	Pts (N = 83), n (%)
$\geqslant$1 dose delay ($\geqslant$7 days)	11 (13)
Due to:	
Non-haem toxicity	9 (11)
Haem toxicity	1 (1)
Pt request	1 (1)
$\geqslant$25% dose reduction	5 (6)
Due to:	
Febrile neutropenia	2 (2)
Other haem toxicity	1 (1)
Non-haem toxicity	2 (2)
Grade 3−4 toxicity overall	38 (46)
Grade 3−4 events in $\geqslant$5% of pts:	
Infections	7 (8)
Myalgia	7 (8)
Febrile neutropenia	4 (5)
Fatigue	4 (5)
Peripheral neuropathy	4 (5)
Nausea	4 (5)

Haem = haematological.

Conclusions: In this study, delivery of ddAC $\rightarrow$ T was feasible with pegfilgrastim and darbepoetin alfa support. There were minimal dose delays $\geqslant$7 days due to haematological toxicity (1/14, 7%) and just 1 transfusion. In CALGB9741, where pts received ddAC $\rightarrow$ T with 7 days of filgrastim and no erythropoietin support, 15% had a dose delay (any duration) due to haematological toxicity and 13% of pts required a blood transfusion.

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Aromatase inhibitor as neoadjuvant hormone therapy for breast cancer

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Background: Aromatase inhibitors block estrogen biosynthesis systemically or in cancer tissues, and are increasingly used to treat postmenopausal women with breast cancer. Here we report the efficacy of aromatase inhibitors and the effect on the expression of hormone receptors and Ki67 in breast cancer tissue.

Methods: 17 postmenopausal patients with operable or locally advanced estrogen receptor (ER) positive breast cancers were treated with anastrozole or exemestane. Biopsies were obtained pre and post treatment and assessed by immunohistchemistry (IHC) for Ki67, ER and progesterone receptor (PgR). Allred IHC score were assigned and categorized as low (0−2), medium (3−5) and high (6−8).

Results: The clinical objective response rate was 70.6%, without progression. Twelve of 17 patients showed partial response (PR) and 5 showed no change (NC). An increased in PgR category in 1 of 12 responding tumors. A decrease in PgR category was more frequent in responding tumors (9 tumours [75%] PR vs. 3 tumors [60%] NC). Percentage change in Ki67 expression from baseline during treatment is 20.4$\pm$13.6% in responding tumors and 138.6$\pm$92.0% in non-responding tumors, respectively. Suppression of the proliferation marker Ki67 was greater in responding tumors than in non-responding tumors.

Conclusion: Neoadjuvant aromatase inhibitor provided satisfactory efficacy and safety profiles in breast cancer. The main biological effects consisted of a reduction in PgR expression for responders and a decrease in Ki67 expression.

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The benefit using an integrated electronical study platform for a presurgical therapy trial (HEDON) in primary breast cancer

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Background: Normally, the capture of clinical trial data is labor intensive and error-prone, requiring data to be transcribed into a paper case report