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Implementation of guidelines for adjuvant endocrine therapy in early breast cancer

Z. Walters[1], S. Rudman[1], A. Rigg[1]. [1]*Guy's and St. Thomas' Hospital, Department of Medical Oncology, London, United Kingdom*

Background: Several large international studies have shown a survival benefit with aromatase inhibitors in patients with hormone-receptor positive early breast cancer (HR+EBC), either alone or sequentially after tamoxifen. Regional and national guidelines have been developed in the UK to inform appropriate use of licensed drugs in HR+EBC. Choice of regimen is influenced by menopausal status and risk of recurrence. Implementation of guidance, particularly ensuring the switch of therapy in appropriate women after 2 or 3 years, is a multidisciplinary challenge.
Materials & Methods: An audit of adherence and implementation of South East London Cancer Network guidelines for adjuvant endocrine therapy was conducted. The multidisciplinary meeting record was used to identify all patients with HR+EBC diagnosed between 1/7/05 – 31/10/05 at Guy's Hospital. Case notes were then used to determine a patient's menopausal status, risk of recurrence and endocrine treatment.
Results: 75 HR+EBC patients were diagnosed in the study period (see Table 1). Post-menopausal high risk and pre-menopausal women were managed according to guidelines, with the exception of 1 pre-menopausal patient who was switched inappropriately. 33% of post-menopausal moderate risk patients who should have switched after 2 to 3 years on tamoxifen had no documented switch. 27% of low risk post-menopausal women were switched unnecessarily to an AI.
Conclusions: The management of adjuvant endocrine therapy in HR+EBC patients was appropriate in the pre-menopausal and high risk post menopausal subgroups. However in low and moderate risk groups some patients did not switch appropriately. This may reflect the nature of an evolving complex evidence base and highlights the need for clear guideline production. In addition responsibility for ensuring switching needs to be clearly allocated within the multidisciplinary team at a local level.

Group	Treatment according to Guidelines	Total number of patients	Number advised appropriate starting treatment	Number suitable for AI switch without switch occurring	Number switched inappropriately to an AI
Pre-menopausal	Tamoxifen 5 years	27	27 (100%)	NA	1 (4%)
Post-menopausal					
Low risk	Tamoxifen 5 years	16	15 (94%)	NA	4 (27%)
Moderate risk	Tamoxifen 2−3 years then switch to Exemestane/Anastrozole	17	11 (65%)	3 (33%)	NA
High risk	Anastrozole/Letrozole 5 years	15	13 (87%)	NA	NA

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Bisphosphonates do not prevent bone fractures in early breast cancer: a meta-analysis

A. Valachis[1], N.P. Polyzos[2], V. Georgoulias[1], D. Mavroudis[1], D. Mauri[3]. [1]*University of Crete, Medical Oncology, Heraklion, Greece;* [2]*PACMeR, Gynaecological Oncology and Obstetrics and Gynaecology, Lamia, Greece;* [3]*General Hospital of Lamia, Medical Oncology, Lamia, Greece*

Background: Recent data suggest that fractures might affect quality of life and survival in early breast cancer patients. Bisphosphonates are effective in treatment and prevention of cancer treatment-induced bone loss, but their value in the prevention of fractures is still investigational. We conducted a systematic review and meta-analysis of randomized clinical trials to evaluate the fracture rate in breast cancer patients receiving adjuvant bisphosphonates compared with those receiving no treatment or placebo.
Methods: Trials were located through PubMed, ISI, Cochrane Library, and major cancer scientific meetings searches. We identified 21 potentially eligible trials. Of these, fourteen studies reported fracture data and were included in the analysis. Overall, 7,461 early breast cancer patients were randomized, 3691 received bisphosphonates and 3770 received either placebo or no treatment.
Results: Adjuvant breast cancer treatment with bisphosphonates did not reduce the fracture rate compared to placebo or no use either in intent to treat analysis (12 trials, OR: 0.99, 95% CI 0.73−1.34, p = 0.932), in comprehensive analysis (all 14 trials included, OR: 0.84, 95% CI 0.65−1.09 p = 0.197), in postmenopausal patients (7 trials, OR: 0.82, 95% CI 0.55−1.20 p = 0.298), and in patients receiving aromatase inhibitors (6 trials, OR: 0.79, 95% CI 0.53−1.17 p = 0.242).
Conclusion: Our meta-analysis provides substantial evidence that bisphosphonates in the adjuvant setting among women with breast cancer do not decrease the number of fractures compared with placebo or no treatment.

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European Cooperative Trial in Operable Breast Cancer II (ECTO II): activity of primary chemotherapy in ER negative early breast cancer

M. Zambetti[1], G. Pascoletti[2], P. Gomez[3], V. Semiglazov[4], A. LLuch[5], E. De Benedictis[1], B. Ojeda[6], C. Dittrich[7], P. Valagussa[8], L. Gianni[1]. [1]*Istituto Nazionale Tumori, Medical Oncology, Milano, Italy;* [2]*Ospedale Santa Maria della Misericordia, Medical Oncology, Udine, Italy;* [3]*Hospital Vall d'Hebron, Medical Oncology, Barcelona, Spain;* [4]*NN Petrov Research Institute of Oncology, Oncology, St. Petersburg, Russian Federation;* [5]*Hospital Clinico Universitario de Valencia, Medical Oncology, Valencia, Spain;* [6]*Hospital Saint Pau, Medical Oncology, Barcelona, Spain;* [7]*Kaiser Franz Josef-Spital, Medical Oncology, Vienna, Austria;* [8]*Fondazione Michelangelo, Operations Office, Milano, Italy*

Background: To improve the pathological complete remission rate documented in the ECTO trial (Clin Cancer Res.2005:8715) we activated a randomized Phase II two-stage protocol with chemotherapy in ER negative early breast cancer >2 cm at diagnosis.
Methods: 127 patients were enrolled from June 2005 to March 2008. Patients were randomly allocated to 3 regimens: A (AT, doxorubicin 60 mg/m^2 + paclitaxel 200 mg/m^2, q 3 w × 4 followed by CMF q 4 w × 4); B (AT as above followed by CM + capecitabine 1850 mg/m^2 for 14 days q 4 w × 4); C (AC, doxo 60 mg/m^2 + cyclophosphamide 600 mg/m^2 q 3 w × 4 followed by paclitaxel 100 mg/m^2 d1+8 + capecitabine as above q 3 w × 4).
Results: All patients were assessed for the first step of the analysis plan. Baseline characteristics (age, menopause, PgR and HER2) were balanced and left ventricular ejection fraction (LVEF) was similar in all 3 groups.
Rates of complete pathological absence of invasive cancer in the breast (pCR) and in the breast and axilla (tnpCR) are reported in the table and would have allowed for expanding to stage 2 only in the case of regimen A.

	Regimen A	Regimen B	Regimen C
# patients	43	41	43
% pCR	53.5 (37.7−68.8)	41.5 (26.3−57.9)	39.5 (25.0−55.6)
% tnpCR	44.2 (29.1−60.1)	36.6 (22.1−53.1)	37.2 (23.0−53.3)

() 95% confidence limits

Treatment was well tolerated. More frequent delays occurred during the last four cycles of each regimen. Grade 3 neutropenia was more frequently observed during AC (8%) than during AT (1%) and one episode of G3 thrombocytopenia was documented during AC. G3 neutropenia was more frequent after paclitaxel and capecitabine (12%) than after CMF (7%) and CMX (7%). CTC 2 LVEF modification during chemotherapy was documented in one patient in each of the study arms. A bank of paraffin embedded biopsies and tumor blocks successfully collected more than 95% of the specimens.
Conclusions: All regimens were feasible and achieved a high rate of pCR in ER-negative tumors. Regimen A was the only one meeting the threshold to move to stage 2 of the study. The combined analysis of pCR rates and feasibility was in line with the findings of the ECTO trial. The study was therefore closed confirming that the sequence of AT and CMF is a feasible and very active therapeutic option for women with early breast cancer.
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Resource-based data availability for erbB2-driven breast cancer in Asian women: experts' opinion

Y. Tan[1], S. Han[2], Y. Lu[3], C. Yip[4], P. Sunpaweravong[5], J. Jeong[6], P. Caguioa[7], S. Aggarwal[8], E. Yeoh[9], H. Moon[9]. [1]*Medical Oncology Centre, Medical Oncology, Singapore, Singapore;* [2]*Inje University Sanggye Paik Hospital, Department of Surgery, Seoul, South Korea;* [3]*National Taiwan University Hospital, Department of Oncology, Taipei, Taiwan;* [4]*University Malaya Medical Centre, Department of Surgery, Kuala Lumpur, Malaysia;* [5]*Songklanagarind Hospital, Department of Oncology, Hat Yai, Thailand;* [6]*Yongdong Severance Hospital, Department of Surgery, Seoul, South Korea;* [7]*Cancer Institute St Luke's Medical Center, Department of Medical Oncology, Quezon City, Philippines;* [8]*Sir Ganga Ram Hospital, Department of Oncology, New Delhi, India;* [9]*GlaxoSmithKline, Oncology R&D, Asia Pacific, Singapore*

Background: Breast cancer incidence is increasing throughout Asia. However, the biological characteristics in Asian breast cancer are not always well understood due to the limited availability of tests and local data plus their inadequate inclusion in global literature databases. Recent

advances in anti-erbB2 treatment requires a better understanding of Asian breast cancer biology, especially, erbB2 status.
Methods: A literature search was conducted in seven Asian countries on breast cancer studies where tumour erbB2 overexpression was assessed. The keywords *erbB2* OR *HER2* OR *ErbB-2* OR *HER-2* AND *breast cancer* AND (*country*) were used to search PubMed, international and local conference abstracts and local-language journals from the year 2000 onwards. Where available, we selected up to five representative studies from each country on the basis of population size, multi-institution patient populations, institution reputation and journal impact factor. The selection of articles was finalized with expert opinion from local breast cancer specialists to ensure objectivity in representation.
Results: The mean or median age ranged from 46−56 years. The limited availability of erbB2 testing in some Asian countries with socio-economic constraints results in limitation of data. Definitions of erbB2 positivity using *immunohistochemistry* (IHC) vary between institutions and *fluorescent in situ hybridization* (FISH) is not routinely performed in several Asian countries. The larger studies in particular confirm that the proportion of erbB2-positive breast cancer in Asia is generally similar to the 20−30% reported for Western women. In most studies that evaluated tumour erbB2 and hormone status, erbB2 over-expression correlated negatively with estrogen receptor (ER) positivity.

erbB2 status in Asian breast cancer studies in 2000 onwards

Country (number of studies reviewed)	Total population (study population range)	Percentage range of erbB2-positive samples	Definition of erbB2 positivity
Korea (5)	14,926 (188−9,668)	24.5−36.9	IHC 2+ plus 3+; or FISH
Taiwan (5)	1,485 (63−1,028)	19.0−38.5	IHC 2+ and/or 3+; FISH
Singapore (5)	802 (97–321)	16.55−34.3	IHC 2+ and/or 3+; FISH
Thailand (4)	5,812 (318−4,546)	17.87−32.0	Positive by IHC
Philippines (1)	2,333	20.0	IHC 3+
Malaysia (2)	699 (306; 393)	34.5; 44.4	IHC 3+; not stated
India (4)	892 (204–271)	25.19−42.0	Positive by IHC

Conclusions: The increased availability of accurate erbB2 testing and data would aid improved treatment of erbB2-positive breast cancer in these countries.

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Prophylactic antibiotics are necessary to minimise the risk of febrile neutropenia in patients receiving TAC chemotherapy

J.E. Scaife[1], P. Jenkins[1]. [1]*Gloucestershire Oncology Centre, Clinical Oncology, Cheltenham, United Kingdom*

Following the publication of the BCIRG001 trial, TAC chemotherapy represents a new treatment standard for early node-positive breast cancer. In randomised trials, myelosuppression is common with this regimen and the rate of febrile neutropenia (FN) has been documented at 6.5−24.7%. Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) plus or minus antibiotics is required. Our previous studies have shown that myelosuppression is much more common in patients treated outside clinical trials in a community hospital setting [1].
Between January 2007 and April 2009, 169 patients at our centre received TAC chemotherapy (docetaxel 75 mg/m^2, doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2, all on day 1, every 3 weeks). The median age was 48 (range 27−66). All patients received primary prophylaxis with subcutaneous pegfilgrastim 6 mg on day 2 of each cycle. For the first 81 patients treated, prophylactic antibiotics were omitted due to local concerns regarding Clostridium difficile infection. The high frequency of FN in this group led us to add levofloxacin prophylaxis in all patients.
29/81 (36%) patients treated with pegfilgrastim alone developed FN and there was one septic death. The rate of FN was significantly lower at 20/88 (23%) in those treated with G-CSF and levofloxacin ($p = 0.044$). The median duration of inpatient stay was 3.5 days (range 1−14 days). In 26 patients (53%), FN occurred during the first cycle. The median time to onset of FN was 7 days (range 2−14) post chemotherapy.
Prophylactic antibiotics significantly reduce the rate of FN and are an important component of the supportive care for patients receiving TAC chemotherapy. Even with antibiotics and G-CSF, the frequency of FN in patients treated outside clinical trials is high, particularly after the first cycle of treatment. Better predictive factors are required to identify patients who are at risk of this complication.

References

[1] Jenkins P et al. Obesity is not associated with increased myelosuppression in patients receiving chemotherapy for breast cancer. Eur J Cancer 2007; 43: 544−8.

5145 POSTER

Success-C-study: simultaneous study of docetaxel based anthracycline free adjuvant treatment evaluation as well as life style intervention strategies

J. Salmen[1], B. Rack[2], P. Hepp[1], D. Chatsiproios[3], A. Schneeweiss[4], H. Sommer[2], W. Lichtenegger[5], M.W. Beckmann[6], W. Janni[1]. [1]*Heinrich-Heine-Universität, Frauenklinik, Düsseldorf, Germany;* [2]*Universität München, Frauenklinik, München, Germany;* [3]*Gemeinschaftspraxis Mannheim, Gynäkologie und Geburtshilfe, Mannheim, Germany;* [4]*Universität Heidleberg, Gynäkologie und Geburtshilfe, Heidelberg, Germany;* [5]*Charité Berlin, Frauenklinik, Berlin, Germany;* [6]*Universität Erlangen, Frauenklinik, Erlangen, Germany*

Background:
- Taxane based chemotherapy, like the PACS 01 regimen (3×FEC followed by 3×Docetaxel) has been established as standard treatment option for early breast cancer
- Anthracycline-based regimens do not seem to be superior in HER2-negative patients (Gennari et al., Slamon et al.)
- Lifestyle-Intervention, including physical activity and a fat-reduced diet, seems to improve the outcome in patients with early breast cancer
- The prognostic relevance of isolated tumor cells in bone marrow has recently been proven (Braun et al., Janni et al.) and early data indicates a prognostic relevance of circulating tumor cells in peripherial blood (Rack et al., ASCO 2008).

Methods: The SUCCESS-C Trial is a prospectively randomized multicenter clinical trial for early, HER2/neu-negative breast cancer patients. The study comprises two sequential randomizations.
Inclusion criteria (in extracts):
- primary epithelial invasive carcinoma of the breast pT1−4, pN0−3, pM0
- no evidence of HER2/neu overexpressing
- histopathological proof of axillary lymph node metastases or high risk node negative disease

Exclusion criteria (in extracts):
- inflammatory breast cancer
- cardiomyopathie which impaired ventricular function and other cardiological problems.

The first randomization of the study will compare the disease-free survival in patients treated with 3 cycles of Epirubicin (100 mg/m^2), Fluoruracil (500 mg/m^2) and Cyclophosphamid (500 mg/m^2), followed by 3 cycles of Docetaxel (100 mg/m^2) versus 6 cycles of Cyclophosphamid (600 mg/m^2) and Docetaxel (75 mg/m^2).
The second randomization examines the benefits of standardized lifestyle dietary intervention and weight reduction, conducted by intensive telephone coaching. The telephone intervention will involve 20 phone calls, as well as mailings and a participant manual.
Adjunct to these interventional strategies is a translational research program, which will focus on the role of CTCs as valuable marker of treatment failure and early disease progression. At three predefined time points during treatment peripheral blood will be drawn.
Results: Results of the toxicity analysis and the translational research program will be available at the end of treatment. First conclusions about the effects on DFS are expected two years after the end of chemotherapeutic treatment or lifestyle intervention respectively.

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Does adjuvant bisphosphonate in early breast cancer modify the natural course of the disease – a meta-analysis of randomized controlled trials

D. Mauri[1], A. Valachis[2], L. Tsali[3], N.P. Polyzos[4], G. Casazza[5]. [1]*General Hospital of Lamia, Medical Oncology, Lamia, Greece;* [2]*University of Heraklion, Medical Oncology, Heraklion, Greece;* [3]*PACMeR, Internal Medicine, Lamia, Greece;* [4]*PACMeR, Gynecological Oncology, Lamia, Greece;* [5]*Universita' degli Studi di Milano, Statistica Medica e Biometria, Milano, Italy*

Background: Preclinical studies demonstrated that bisphosphonates may have antitumour activity in addition to their ability to reduce osteoclast-mediated bone resorption.
Aim: To address whether use of bisphosphonates in breast cancer adjuvant setting might have any effect on overall survival, prevention of disease recurrences and bone metastases occurrence.
Study design: Systematic review and meta-analysis of randomized controlled trials **Methods:** Trials were located through PubMed, ISI, Cochrane Library, and major cancer scientific meetings searches.
Result: Data eligible for our analyses could be retrieved for 13 studies evaluating the adjuvant use of bisphosphonates compared with no use. Pooled results showed no statistical significant differences with the use