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.

5144 POSTER

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

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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

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5145 POSTER

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

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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.

5146 POSTER

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

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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

of bisphosphonates in early breast cancer versus non use for the overall number of deaths (summary OR: 0.708, 95% CI: 0.482 to 1.041, *P*-value = 0.079), disease recurrences (summary OR: 0.843, 95% CI: 0.602 to 1.181, *P*-value = 0.321), and bone metastases (summary OR: 0.925, 95% CI: 0.768 to 1.114, *P*-value = 0.413). Conversely, adjuvant treatment with bisphosphonates was not associated with any statistical significant difference for type of recurrences: distant metastases (OR = 0.896, 95% CI 0.674−1.192, p = 0.453), visceral recurrences (OR = 1.051, 95% CI 0.686−1.609, p = 0.820) and local relapses (OR = 1.056, 95% CI 0.750−1.487, p = 0.756).
Conclusion: Current available randomized evidence do not support the hypothesis that use of bisphosphonates in adjuvant treatment of early breast cancer is likely to alter the natural course of the disease. Nonetheless there seems to be a non significant trend for better outcomes in patients receiving treatment. Until further evidence from new trials will become available adjuvant bisphosphonates should not be routinely recommended as agents that may potentially alter the course of disease in breast cancer adjuvant setting.

5147 POSTER

Taste and smell changes in patients receiving chemotheraphy for breast cancer

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Background: Taste and smell changes are much more prevalent in patients undergoing chemotheraph. The literature yields little information on taste and smell changes. In this study, the frequency and features of these changes were evaluated in patients receiving chemotheraphy for breast cancer.
Patients and Methods: Seventy-four women receiving chemotheraphy in out-patient chemotheraphy unit were evaluated with quastionnaire about taste and smell changes.
Results: The mean age was 49.76 (33−74). The most frequently administired chemotheraphy regimens were antracyclines (50 patients), taxanes (13 patients single drug, 4 patients in combinations) and platinum containing regimens (7 patients). Taste and smell dysfunction was reported by 65 (90.2%) and 61 (82.4%) patients, respectively. Forty-eight patients (96%) treated with antracyclines reported taste changes, while 45 patients (90%) were reported smell changes. These rates for single agent taxanes were 10 (76.9%) and 9 (69.2%) patients, respectively. Six patients (85.7%) treated with platinum containing regimens reported both taste and smell changes. Increased sensitivity to odors was reported by 45 patients (73.7%) and 16 patients reported decreased sensitivity. Taste changes were described as bitter (26 patients), metallic (25 patients), sour (10 patients) and salty (4 patients). Forty-five patients (69.2%) informed their families and health professionals about these changes. Meat and fish products were the most common undesired foods for 31 patients, followed by dairy products for 13 patients. Forty-one (63%) patients had not taken any measures against these changes. But 24 patients had taken some measures like increased water intake, some spices and souces.
Forty-four patients (65.2%) reported that taste and smell changes were the most severe during chemotheraphy administration.
Conclusions: Much more research is needed to understand the nature, frequency, severity and duration of taste and smell alterations and their significance for the quality of life of cancer patients. Interventions to alter taste and smell changes may improve the outcome of cancer therapy, reduce the cost of care, and improve the quality of life of these patients.

5148 POSTER

Emerging recommendations for the prevention of cancer treatment-induced bone loss in women with breast cancer

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Background: Cytotoxic chemotherapy, ovarian ablation/suppression, and endocrine therapies reduce estrogen levels, causing rapid bone loss and increasing fracture risk in women with breast cancer. Bisphosphonates have demonstrated efficacy for preventing cancer treatment-induced bone loss (CTIBL). Several independent recommendations for managing CTIBL in women with breast cancer have been published. Although not specifically for women with breast cancer, guidelines for treating postmenopausal osteoporosis (PMO) based on data from large population-based studies provide the foundation for overall fracture risk assessment.
Material and Methods: A systematic review was performed to identify recommendations related to CTIBL and PMO in published literature and society guidelines. Diagnosis and treatment recommendations were compared and evaluated for similarities and differences regarding risk assessment and treatment thresholds to identify common trends.
Results: In the past, World Health Organization PMO guidelines and American Society of Clinical Oncology CTIBL guidelines relied on bone mineral density (BMD) as the primary indicator of fracture risk and need for therapy. Recently, guidelines have begun to include clinical risk factors as part of fracture risk assessment. For example, the FRAX algorithm for PMO further refines fracture risk assessment using BMD and clinical risk factors to determine the 10-year probabilities of hip and major osteoporotic fractures. In the breast cancer setting, recently published consensus recommendations suggest evaluating clinical risk factors, such as age, aromatase inhibitor use, family fracture history, corticosteroid or alcohol use, and smoking, with or without BMD to determine whom to treat.
Conclusions: The emerging consensus is that BMD alone is not sufficient to evaluate patient fracture risk and direct treatment decisions. Although BMD cutoff points vary slightly between guidelines, most recommendations now use overall fracture risk (clinical risk factors with or without BMD) to determine who requires preventive therapy. Therapy options for CTIBL include calcium and vitamin D supplementation, lifestyle advice, and bisphosphonate therapy based on degree of fracture risk. Individualized fracture risk assessment will allow more proactive management of bone health in patients with breast cancer.

5149 POSTER

Randomized phase II trial of preoperative chemotherapy plus lapatinib, trastuzumab or both in HER2 positive breast cancer: results of the first step simon's design

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Introduction: This is a randomized phase II trial of preoperative chemotherapy (CT) with sequential taxanes-anthracyclines combined with trastuzumab, lapatinib, or both trastuzumab and lapatinib in HER2 positive, stage II-IIIA breast cancer patients. Primary end point of the study is the percentage of pathological complete response (pCR) as defined as complete disappearance of invasive tumor in breast and axillary nodes.
Methods: CT consists of sequential paclitaxel 80 mg/m^2 weekly $\times$12 followed by $FE_{75}C$ $\times$4 courses every 3 weeks. In arm A CT is combined with weekly trastuzumab; in arm B CT is combined with lapatinib 1500 mg po daily; in arm C CT is combined with weekly trastuzumab+ lapatinib 1000 mg po daily. Both trastuzumab and lapatinib are started concomitantly with the first paclitaxel dose, and are administered throughout the duration of CT. Following the second safety report of the Independent Data Monitoring Committee, the protocol has been amended by reducing lapatinib dose at 1250 mg in arm B and at 750 mg in arm C, due to the occurrence of grade 3 diarrhoea in 20% and in 41% of the patients randomized to arm B and C respectively. The study sample size has been calculated according to the two steps Simon's design. The first stage includes 52 patients: at least 4/17 pCRs in arm A, 4/17 pCRs in arm B and 8/18 pCRs in arm C are needed to proceed to the second step. The overall planned accrual is120 patients.
Results: 62 patients have been randomized: 20 in arm A, 19 in arm B, and 23 in arm C. Median age is 49 years (range 27−66). Clinical stage at diagnosis: IIA in 35%, IIB in 49%, and IIIB 16%. Forty-four patients underwent surgery, and are evaluable for response: 67% of the patients received breast conserving surgery. A pCR in breast and axillary nodes has been observed in 17 patients (39%). Left ventricular ejection fraction (LVEF) has been evaluated at baseline, after 12−13 weeks, and at the end of therapy. Mean LVEF% (range) was 61.8% (52%-77%), 61.1% (50%-78%) and 61% (53%-77%) respectively. No clinically relevant cardiac events were observed. One patient in arm A experienced a drop of 24 percentage points from baseline at the end of therapy, still remaining above the limit of normal.
Conclusions: The study accrual is ongoing. The results of the first step Simon's design per treatment arm will be presented at the Meeting.