patient (0.6%) on tam and 6 patients (1.9%) were receiving an AI with a moderate inhibitor. 24 patients (16.5%) on tam and 40 patients (12.4%) receiving an AI were receiving weak CYP2D6 inhibitors.

Conclusion: While infrequent, breast cancer patients receive medications that can have an adverse effect on tam therapy, primarily its metabolism and activation. Patients receiving AI therapy do receive medications that can interact with tam metabolism, and as such can be a challenge to manage if they have to change from an AI to tam if they cannot tolerate an AI. This is not an infrequent event as our centre has shown that up to 20% of breast cancer patients discontinue AI's due to side effects. Patients are frequently receiving moderate to weak inhibitors of CYP2D6, and these patients should be tested for their pharmacogenomic profile prior to initiating tam to determine if they are wild-type vs intermediate or poor metabolizers.

14 Poster

Influence of zoledronic acid on bone mineral density in premenopausal women with hormone receptor positive or negative breast cancer and neoadjuvant or adjuvant chemotherapy or endocrine treatment

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Background: Depending on baseline bone mineral density (BMD), adjuvant chemotherapy or endocrine therapy of premenopausal breast cancer patients can lead to a substantially increased risk of osteoporotic fractures. Hereby, a significant decrease of BMD > 10% after 2 years of therapy has been reported. Adjuvant therapy with zoledronic acid (Zometa®) in early breast cancer was investigated in the ABCSG-12 and the Zo-Fast trial. Zoledronic acid 4 mg given every six months increased BMD in premenopausal and postmenopausal women receiving endocrine treatment. In addition, a significant increase in PFS could be observed in favor of zoledronic acid.

Material and Methods: The goal of the two monocentric, placebo-controlled, randomized studies Probone I and Probone II is to demonstrate that adjuvant therapy with zoledronic acid improves BMD in premenopausal women. Hormone receptor negative patients (Probone I) are treated with (neo)adjuvant chemotherapy, hormone receptor positive patients (Probone II) with endocrine treatment alone or in combination with (neo)adjuvant chemotherapy. Patients receive zoledronic acid or placebo i.v. every 3 months for 2 years. Primary objective is the change in BMD at the lumbar spine between baseline and month 24 (measured by DXA). Secondary objectives include disease free survival, BMD at total hip and os calcis, BMD measured by QUS at os calcis and phalanges, markers of bone turnover, pathologic fractures, safety and tolerability. BMD is measured at baseline, 12 and 24 months. QUS and markers of bone turnover are measured at baseline, 3, 6, 12 and 24 months.

Results: Recruitment has been finished in 2009 and 71 hormone receptor positive and 11 hormone receptor negative patients have been enrolled into the studies. 30 out of 82 patients have already finished treatment. The design of the study and demographic data of the enrolled patients will be presented.

Conclusion: Probone I/II are two ongoing studies to evaluate the effect of adjuvant zoledronic acid on BMD in premenopausal patients with breast cancer receiving chemotherapy and/or endocrine therapy. The results of these studies will be of great interest for daily practice because of the lack of approved treatments for the prevention of cancer treatment or aromatase inhibitor induced bone loss in patients with early breast cancer.

15 Poster

Five years of exemestane as initial therapy compared to tamoxifen followed by exemestane for a total of 5 years: the TEAM trial, a prospective, randomized, phase III trial in postmenopausal women with hormone receptor-positive early breast cancer

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Background: Exemestane (E) is a steroidal Aromatase Inhibitor (AI) with an established role in early breast cancer after 2−3 years of Tamoxifen (T). Additionally, AIs have shown superiority to T as initial adjuvant therapy. The Tamoxifen Exemestane Adjuvant Multinational (TEAM) study has been prospectively designed to compare the role of E as initial adjuvant therapy with a sequential approach of T followed by E.

Methods: Postmenopausal patients with hormone receptor-positive early breast cancer were randomized to open-label E 25 mg/d or T 20 mg/d. All patients completed surgery and chemotherapy, if indicated. Data were collected and analyzed by the Central Data Center in Leiden, The Netherlands. The trial was initiated in 2001 with the primary objective being a comparison of disease-free survival (DFS) with T vs. E. In 2004, TEAM was modified in response to new data; all those initially receiving T were switched to E after 2.5−3 years. An additional 2500 patients were recruited and randomized at diagnosis to E or T followed by E for 5 years. The modified study design included 2 co-primary analyses: (1) DFS of T vs. E that was previously reported at 2.75 years follow-up and (2) DFS at 5 years follow-up of E vs. T followed by E.

Results: Between 2001 and January 2006, 9779 women were randomized to TEAM. In total, 99% of patients were ER+ and/or PgR+, 50% were node-negative, 44% underwent mastectomy, 68% received radiotherapy, and 36% received chemotherapy. Median follow-up is now 5.1 years. There were 712 DFS events in E vs 714 in T followed by E (locoregional or distant recurrence, second breast cancers, or death without recurrence); HR 0.97 (95% CI 0.88–1.08; p-value 0.60). There were 400 patients with distant metastases in E vs 420 in T followed by E; HR 0.93 (95% CI 0.81–1.07; p-value 0.30). No additional safety issues have emerged with longer follow-up.

Conclusion: Overall this trial shows that starting with E is not more effective than T followed by E in preventing breast cancer recurrence. The previously reported significant improvement in distant recurrence with E vs. T at 2.75 years has not been maintained with longer follow-up after switching from T to E. This suggests that for postmenopausal patients with endocrine sensitive early breast cancer the use of either 5 years of upfront E or T followed by E are appropriate treatment options.

16 Poster

Circulating tumour cells (CTCs) can be detected in peripheral blood of breast cancer (BC) patients two years after primary diagnosis

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Background: Recent trials have demonstrated prognostic relevance of CTCs in metastatic BC. The SUCCESS trial evaluates the role of CTCs at primary diagnosis and after chemotherapy as well as two and five years after diagnosis in primary BC patients treated with chemotherapy and zoledronate.

Methods: We analyzed 23 ml of peripheral blood in N+ and high risk N− primary BC pts receiving 3×FEC (500/100/500)–3×Doc100 q3w vs. 3×FEC (500/100/500)–3×DocGemcitabine (75/1000 d1+8) chemotherapy

followed by 2 yrs (4 mg q3m×24m) vs. 5 yrs (4 mg q3m×24m followed by q6m×36m) of zoledronate. CTC results after two years are shown. CTCs were assessed with the CellSearchSystem (Veridex, Warren, USA). After immunomagnetic enrichment with an anti-Epcam-antibody, cells were labelled with anti-cytokeratin (8,18,19) and anti-CD45 antibodies.

Results: The data of 579 pts at the mean of 29 months (range 20−43) after diagnosis are available. 4.3% of pts (n = 25) presented with >1CTC in peripheral blood. In pts with the detection of CTCs, the mean number of cells was 1 (range 1−29). While we found 1 CTC in 5.9% and 2 CTCs in 1.6% of pts, 1.5% had 3−5 CTCs, 1.2% >5 CTCs. We found no correlation between the presence of >1CTC with tumor size (p = 0.41), nodal status (p = 0.41), grading (p = 0.45), hormonal status (p = 0.92) or Her2-status of the tumor (p = 0.59).

In this patient group, 9.7% and 6.9% of pts had presented with >1CTC at primary diagnosis and after chemotherapy, respectively. We found no correlation of CTCs after chemotherapy with the results at primary diagnosis (p = 0.08) or at two years (p = 0.23). However, the presence of CTCs at diagnosis was associated with CTCs after two years (p = 0.03).

In 184 postmenopausal HR+ pts endocrine treatment data was analyzed. CTCs at two years were detected in 6.8% of pts on tamoxifen (n = 9), while 1.9% of pts were positive on anastrozole treatment (n = 1; p = 0.19).

Conclusions: The SUCCESS trial is the first randomized chemotherapy trial prospectively evaluating the role of CTCs in a large cohort of primary breast cancer patients. CTCs were detected in a relevant number of recurrence-free patients persisting after cytostatic, endocrine and zoledronate treatment. Longer follow-up will deliver insight in their prognostic relevance.

17 Poster

Inclusion criteria for the use of neoadjuvant chemotherapy in breast cancer

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Background: Only patients with pathological complete response (pCR) and patients in need of mastectomy before but receiving breast conservation (BCT) after successful neoadjuvant chemotherapy (nCT) really benefit from this treatment. The aim of this study was to find predicting factors for pCR and BCT to define better individualized criteria for neoadjuvant chemotherapy.

Method: All consecutive patients who had received standardized neoadjuvant chemotherapy in several prospective trials, and operated on between 1995 and 2007 after nCT were included in this retrospective analyses. For nCT either 3 cycles of CMF or 4−6 cycles of EC were used. Patients with her2neu overexpression received Herceptin adjuvant.

Results: 308 patients were included in the final analyses. Median follow up was 60 months. Patients with a documented pCR (11%) had a trend for improved overall survival (OS; 100% versus 86% p = 0.07) and distant recurrence free survival (DRFS; 92% versus 72% p = 0.08). Patients after BCT had a significant better OS (93% versus 78%) and DRFS (83% versus 62%) compared with patients after mastectomy (p = 0.0001) at a median follow up of 60 months. Multivariate analyses demonstrated that predictors for pCR were ductal histology (p = 0.01), endocrine non-responsive (p = 0.0001) and HER-2/neu positive (p = 0.007) breast cancer. Smaller size tumors tended to have a higher chance for pCR (11% versus 6% p = 0.07). A clinical complete response was predictive for the use of BCT (p = 0.0001). No other biological marker such as tumor type, grading or endocrine responsiveness was predictive for the use of BCT. Endocrine non-responsive ductal type breast cancers with HER-2/neu overexpression were most likely to achieve a pCR while lobular (1.5% of all lobular versus 9% of all ductal; p = 0.03), endocrine responsive breast cancers (3.6% of all endocrine responsive versus 14% of all endocrine non responsive; p = 0.0006) had reduced chances for a pCR. However, patients with lobular and/or endocrine responsive breast cancer still showed an increase in breast conservation of 30%.

Conclusion: Indications for neoadjuvant chemotherapy are surgical need for mastectomy including lobular and endocrine responsive breast cancer OR ductal type, endocrine non-responsive breast cancer of any size. Moreover, patients with her2neu positive breast cancer should also be treated preoperatively, because of the high likelyhood of these cancers to respond very well.

Wednesday, 24 March 2010 18:15–19:15

POSTER SESSION

Adjuvant and neo-adjuvant therapy

18 Poster

Biological activity of a combination of fulvestrant 500 mg (F500) plus anastrozole versus F500 alone or anastrozole alone as neoadjuvant treatment for breast cancer

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Background: Fulvestrant is an oestrogen receptor (ER) antagonist with no agonist effects that leads to dose-dependent reductions in tumour biomarkers (ER, progesterone receptor [PgR] and Ki67 levels). Combining fulvestrant with an oestrogen-lowering agent such as anastrozole may lead to a greater ER blockade and anti-tumour activity. This study compared the biological activity of fulvestrant 500 mg (F500) plus anastrozole (A) vs F500 alone or A alone as neoadjuvant treatment in postmenopausal women with ER-positive, primary breast cancer.

Methods: This was a Phase II, double-blind, randomised, multicentre trial (9238IL/0057; NCT00259090). Eligible patients were randomised 1:1:1 to receive: F500 (2×250 mg on Day 1) plus A 1 mg once daily (od) for 14−21 days (F500+A); F500 plus anastrozole placebo od for 14−21 days (F500); or A 1 mg od plus fulvestrant placebo for 14−21 days (A). Tumour biopsy samples were taken pre-treatment and at surgery to assess changes in ER, PgR and Ki67 index (evaluated by non-automated H-score assessment; treatment differences assessed by analysis of covariance). Tolerability (incidence of adverse events [AEs]) was a secondary endpoint.

Results: In total, 121 patients were randomised; 99 paired samples were analysed. Treatment with F500, F500+A and A significantly reduced the mean ER index from baseline (−41%, −35% and −15%, respectively; all p < 0.001). Compared with A, F500 and F500+A led to greater reductions in ER index (p = 0.0001 and p = 0.0004, respectively). There was no additional reduction in ER index with F500+A vs F500 alone (p = 0.21). For Ki67 and PgR, there were no between-treatment differences. PgR and Ki67 were significantly reduced from baseline in all groups (Ki67: −81%, −85% and −89%; PgR: −37%, −44% and −42% for F500, F500+A and A, respectively; all p = 0.0001). The incidence of AEs was similar for all treatment groups.

Conclusions: This study is the first to investigate the biological activity of fulvestrant 500 mg with and without anastrozole in a neoadjuvant setting. Treatment effects on the ER confirm the different modes of action reported experimentally for these agents. F500 alone or F500+A both significantly decreased ER index, but there was no further impact on ER by combining F500+A. No additional reductions in PgR and Ki67 levels were observed with F500+A vs F500 alone. These data suggest that it is unlikely there is a benefit of combining A with F500 in terms of biological activity in the neoadjuvant setting.

19 Poster

Cost-effectiveness of adding zoledronic acid to endocrine therapy in premenopausal women with hormone-responsive early breast cancer in Portugal, Spain, and Italy, based on the ABCSG-12 Study

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Background: To estimate the cost-effectiveness of adding zoledronic acid (ZOL) 4 mg intravenously q6m to adjuvant endocrine therapy (ET) in premenopausal women with hormone-responsive early breast cancer (HR+EBC) from the perspectives of the healthcare systems in Portugal, Spain, and Italy, respectively.

Material and Methods: A Markov model was used to project lifetime outcomes and costs of breast cancer care for premenopausal women with