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

O. Riedl[1], M. Mittlboeck[2], G. Steger[3], R. Bartsch[3], M. Rudas[4], P. Dubsky[1], R. Jakesz[1], M. Gnant[1], F. Fitzal[1]. *[1]Allgemeines Krankenhaus der Stadt Wien, General Surgery, Vienna, Austria; [2]Allgemeines Krankenhaus der Stadt Wien, Biostatistic, Vienna, Austria; [3]Allgemeines Krankenhaus der Stadt Wien, Oncology, Vienna, Austria; [4]Allgemeines Krankenhaus der Stadt Wien, Pathology, Vienna, Austria*

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

J.F.R. Robertson[1], J.M. Dixon[2], D.M. Sibbering[3], A. Jahan[4], I.O. Ellis[5], E. Channon[6], R.I. Nicholson[7], J.M.W. Gee[7]. *[1]Nottingham University, Division of Breast Surgery, Nottingham, United Kingdom; [2]Western General Hospital, Breast Unit, Edinburgh, United Kingdom; [3]Derby City General Hospital, Breast Unit, Derby, United Kingdom; [4]Kingsmill Hospital, Division of Surgery, Mansfield, United Kingdom; [5]University of Nottingham, School of Molecular Medicine, Nottingham, United Kingdom; [6]Chirostat, Nottingham, United Kingdom; [7]Cardiff University, Welsh School of Pharmacy, Cardiff, United Kingdom*

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

T.E. Delea[1], C. Tanaja[1], S. Kaura[2], P. Sternini[3], S. Gerzeli[4], M. Gnant[5]. *[1]Policy Analysis Inc. (PAI), Brookline, USA; [2]Novartis Pharmaceuticals Inc., Oncology Global Health Outcomes Research, Florham Park, USA; [3]Novartis Farma S.p.A, Origgio, Italy; [4]Department of Applied Statistics and Economics "Libero Lenti" University of Pavia, Applied Statistics and Economics, Pavia, Italy; [5]Department of Surgery Medical University of Vienna, Surgery, Vienna, Austria*

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

HR+EBC receiving 3 y of goserelin and (1) adjuvant ET (tamoxifen or anastrozole); or (2) adjuvant ET plus ZOL q6m. Cost-effectiveness was measured as the incremental cost per quality adjusted life year (QALY) gained. Probabilities of breast cancer recurrence were from the Austrian Breast and Colorectal Cancer Study Group Trial 12 (ABCSG-12). Other probabilities and costs specific to each country were from the published literature. Results were generated under two scenarios: (1) benefits of ZOL persist to the 7-y maximum follow-up in ABCSG-12 (trial benefit); (2) benefits persist until recurrence or death (lifetime benefit).

Results: Expected costs of 3 y of ZOL q6m (medication and administration) were €2,300 for Portugal, €2,100 for Spain, and €1,500 for Italy. Under the trial benefits scenario, these costs were partially offset by savings in treatment of breast cancer recurrence of €200 for Portugal and €900 for both Spain and Italy. ZOL was therefore projected to increase total costs by €2100 for Portugal, €1300 for Spain, and €600 for Italy. Projected QALYs gains with ZOL were 0.33 for Portugal, 0.47 for Spain and 0.46 for Italy. Cost per QALY gained was €6364 for Portugal, €2766 for Spain, and €1304 for Italy (all favorable). Assuming lifetime benefits, savings from preventing breast cancer recurrences completely offset ZOL costs for Spain and Italy, with ZOL yielding net savings of €2100 and €2900 respectively. Incremental total costs were €1400 for Portugal. Projected QALYs gains with ZOL were 0.96 for Portugal, 1.59 for Spain, and 1.57 for Italy. ZOL was therefore dominant (lower costs and more QALYs) for Spain and Italy; the cost per QALY gained for Portugal was highly favorable (€1,458).

Conclusion: Adding ZOL to ET in premenopausal women with HR+EBC is highly cost-effective (<€50,000 per QALY gained) from the healthcare system perspectives of Portugal, Spain, and Italy even under conservative assumptions regarding duration of ZOL benefits. ZOL may be cost saving in Italy and Spain if benefits persist >7 years.

20 Poster

Impact of fulvestrant 500 mg/month versus fulvestrant 250 mg/month on bone turnover markers and endometrial thickness: findings from the NEWEST study

I. Kuter[1], R. Hegg[2], C.F. Singer[3], R.A. Badwe[4], E.S. Lowe[5], U.A. Emeribe[5], E. Anderson[6], F. Sapunar[6], J. Bines[7], N. Harbeck[8]. *[1]Massachusetts General Hospital, Boston, USA; [2]University of São Paulo and Hospital Pérola Byington, School of Medicine, São Paulo, Brazil; [3]Medical University of Vienna, Division of Special Gynecology, Vienna, Austria; [4]Tata Memorial Hospital, Mumbai, India; [5]AstraZeneca, Wilmington, USA; [6]AstraZeneca Pharmaceuticals, Macclesfield, United Kingdom; [7]Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [8]University of Cologne, Breast Center Department of Obstetrics and Gynecology, Cologne, Germany*

Background: Fulvestrant (FASLODEX™) is a selective oestrogen receptor (ER) antagonist with no agonist effects used to treat postmenopausal women with advanced breast cancer at 250 mg/month (F250). Studies have suggested that increasing the dose may enhance ER blockade and improve efficacy. The NEWEST (Neoadjuvant Endocrine Therapy for Women with Estrogen-Sensitive Tumours) study compared the activity of a higher-dose fulvestrant regimen (F500, 500 mg/month plus 500 mg on Day 14 of Month 1) with F250 as neoadjuvant therapy. To collect further tolerability data for F500 vs F250, their effects on bone and endometrium were investigated.

Material and Methods: NEWEST was a Phase II, randomised, open-label, multicentre, 16-week study (9238IL/0065/NCT00093002) of F500 vs F250 in postmenopausal women with ER+, locally advanced breast cancer. Secondary objectives included comparisons of F500 vs F250 on tolerability, endometrial thickness and serum bone markers. Adverse events (AEs) were recorded throughout the study. Changes from baseline to week 16 in endometrial thickness were assessed by transvaginal ultrasound. Serum bone turnover markers (bone-specific alkaline phosphatase [ALP], C-terminal telopeptides of Type 1 collagen [CTX-1] and procollagen Type 1 N propeptide [PINP]) were measured at baseline and every four weeks until surgery (week 16).

Secondary outcome measure	n	Fulvestrant F500 (N = 107)	n	Fulvestrant F250 (N = 101)
Treatment-related SAEs, n (%)		1 (0.9)		3 (3.0)
Treatment-related AEs, n (%)		40 (37.4)		31 (30.7)
Mean change in endometrial thickness (mm), from baseline to week 16				
Patients with any baseline value	46	−1.34	44	−1.10
Patients with baseline value ⩽5 mm	37	−0.03	30	−0.18
Mean change in bone turnover markers, from baseline to week 16				
ALP (μg/L)	73	−0.36	73	−0.15
CTX-1 (ng/mL)	71	+0.02	70	+0.04
PINP (μg/L)	72	−0.35	72	+0.35

Results: In total, 211 women participated (F500 109; F250 102). Key tolerability data are shown below. Treatment-related serious AEs (SAEs) were rare; none led to withdrawal. From baseline to week 16, there were small, non-significant reductions in endometrial thickness (any baseline value) in both treatment groups. Bone turnover markers remained stable throughout the study.

Conclusions: F500 and F250 were well tolerated, with no adverse effects on endometrial thickness or bone turnover markers, indicating no ER agonist effects. The lack of impact on bone suggests a potentially good long-term tolerability profile for F500.

22 Poster

First interim analysis of a randomized trial comparing capecitabine/epirubicin/cyclophosphamide (XEC) vs 5-FU/epirubicin/cyclophosphamide (FEC) as adjuvant therapy for medium- or high-risk early breast cancer (EBC)

Z. Shao[1], B. Huang[2], J. Zhang[3], S. Zhou[4], P. He[5], D. Chen[6], S. Cui[7], C. Ren[8], L. Cai[9], J. Shi[10]. *[1]Cancer Hospital, Department of Breast Surgery, Shanghai, China; [2]Anhui Medical School Affiliated Hospital, Department of Breast Surgery, Hefei, China; [3]Tianjing Cancer Hospital, Department of Breast Surgery, Tianjing, China; [4]Xiamen First Hospital, Department of Breast Surgery, Xiamen, China; [5]Shanghai Sixth People's Hospital, Department of Surgery, Shanghai, China; [6]Yunnan Province Cancer Hospital, Department of Breast, Kunming, China; [7]Henan Province Cancer Hospital, Department of Breast Surgery, Zhengzhou, China; [8]Shanghai Huashan Hospital, Department of Surgery, Shanghai, China; [9]Heilongjiang Cancer Hospital, Department of Oncology, Shanghai, China; [10]Changhai Hospital, Department of General Surgery, Shanghai, China*

Background: Capecitabine is widely used as first-line therapy for metastatic breast cancer because of its high efficacy and good tolerability. Anthracyclines combined with 5-FU and cyclophosphamide are now a post-operative standard of care for medium-/high-risk EBC. We are comparing safety and efficacy of capecitabine or 5-FU combined with epirubicin and cyclophosphamide as postoperative (adjuvant) chemotherapy for EBC.

Patients and Methods: Women with node-positive or high-risk node-negative EBC are eligible for the trial. The planned sample size is 1000 patients (500 in the XEC arm, 500 in the FEC arm). The primary study objectives are to evaluate safety (NCI CTC version 3.0) and to assess 1-, 2-, and 3-year disease-free survival (DFS) rates. Overall survival is a secondary endpoint. Patients are randomised to receive either XEC (capecitabine 1000 mg/m^2 bid, d1−14 + epirubicin 75−90 mg/m^2 iv, d1 + cyclophosphamide 600 mg/m^2 iv, d1) or FEC (5-FU 500 mg/m^2 iv, d1 + epirubicin 75−90 mg/m^2 iv, d1 + cyclophosphamide 600 mg/m^2 iv, d1). In both arms, treatment is given every 3 weeks for up to 6 cycles. After completion of adjuvant chemotherapy, patients can receive radiotherapy at the investigator's discretion. Patients with hormone receptor-positive disease may receive endocrine therapy after completing adjuvant chemotherapy.

Results: By May 2009, 246 patients had been enrolled in the XEC arm and 209 in the FEC arm, all of whom are included in the intent-to-treat analysis reported here. The baseline characteristics are well balanced in the two treatment arms. After 2 years' follow-up, 1- and 2-year DFS rates are 89.24% and 61.78%, respectively, in the XEC arm, and 84.69% and 33.12%, respectively, in the FEC arm. 1-year overall survival rates are 96.03% with XEC and 93.68% with FEC. The two regimens show differing safety profiles. The incidences of all-grade adverse events with XEC and FEC, respectively, are: alopecia (6% vs 11%); hand-foot syndrome (4% vs 0%); and upper respiratory tract infection (0% vs 1%). Severe adverse events to date are neutropenia (2 cases with XEC vs 4 cases with FEC) and abnormal hepatic function (2 cases vs 0 cases, respectively). There have been no cases of severe hand-foot syndrome.

Conclusions: These interim results suggest that the risk of breast cancer recurrence can be reduced by replacing 5-FU with capecitabine in an anthracycline-based adjuvant regimen. The high activity of XEC is achieved with good tolerability.

23 Poster

Pregnancy-associated breast cancer is as chemosensitive as classic breast cancer in the neoadjuvant setting

R. Rouzier[1], G. Werkoff[1], C. Uzan[2], O. Mir[3], J. Gligorov[4], F. Goffinet[5], J.M. Treluyer[6], S. Uzan[1], S. Delaloge[7]. *[1]Hôpital Tenon, Ob Gyn, Paris, France; [2]Institut Gustave Roussy, Surgery, Paris, France; [3]Hôpital Cochin, Oncology, Paris, France; [4]Hôpital Tenon, Oncology, Paris, France; [5]Hôpital Cochin, Ob Gyn, Paris, France; [6]Hôpital Cochin, Pharmacology, Paris, France; [7]Institut Gustave Roussy, Oncology, Paris, France*

Purpose: To determine the chemosensitivity of pregnancy-associated breast cancer (PABC) in the neoadjuvant setting.