struction, the needs of partners and children, hormone replacement therapy and sexuality and fertility issues to be addressed, as part of treatment and care. There has been an important, albeit largely informal, alliance forged between nurses (who are predominantly women) and women with breast cancer to foster better care.

However, health care and more specifically, cancer services are changing. Contemporary health policy emphasises that women as users of health care should be given a direct voice in determining the shape of services and in making key decisions about their own care. Nurses themselves are being given greater responsibility for delivering care and treatment and may increasingly be leading diagnostic and follow-up services where there will be less direct involvement of doctors. This raises questions about the purpose and desirability of intermediaries between women and their doctors, or the necessity of "advocacy" for women with breast cancer since these may reinforce the status quo rather than promoting different doctor-patient relations and nurses are in any case part of the treatment "establishment". There is also greater questioning of the precise role of specialist nurses and insufficient research available to direct the deployment of specialist nurses. New roles and relationships need to be defined, a focus on evolving the roles of specialist nurses may be fruitful in radically altering the shape of breast cancer services so that they may evolve into the "women centred" services we all desire.

200 INVITED

How recruiting patients to clinical trials affects the doctor/patient relationship

K. Pritchard. *Toronto Sunnybrook Cancer Cntr., Division of Clinical Trials and Epidemiology, Toronto, Canada*

The effect of recruitment to clinical trials on the doctor-patient relationship is an under-researched area. There is considerable literature examining the quality of informed consent in cancer clinical trials (Joffe M., Lancet 358: 1772-1777, 2001). Most of this however focuses on patient satisfaction with the informed consent process and on patient understanding of the general principles and details that have been supposedly explained to them as part of informed consent (Tattersall M.H., Lancet 358: 1742-1743, 2001). It has been demonstrated that a patient is more likely to agree to participate in a clinical trial if his or her oncologist explains the items included in the informed consent document, and if the oncologist communicates in a reflective, patient-centered, supportive and responsive manner (Albrecht J.L., J Clin Oncol 17: 3324-3332, 1999).

In randomized trial discussions, the physician must begin by explaining the uncertainty surrounding treatment decisions for each patient. It seems clear that this approach alone must affect a patient's understanding of her physician's approach to her situation. The additional time taken surrounding this interaction, by both physicians and nurses, may however provide considerable positive benefit for patients involved in trial recruitment. Some investigators working in this area feel that the accrual process is in fact "embedded within" the longer-term relationship between the physician and the patient, and that the interaction occurring during the consent process is part of an "alliance building" that is built into the ongoing relationship (Ruckdeshel, J.C., J Cancer Edu 11: 73-79, 1996). Certainly, the additional time taken and information given at trial entry, and subsequently through the trial process would seem likely to be generally beneficial for most patients. If the purpose of the trial, the alternatives to trial entry and the risks and benefits of being involved in the trial are clearly explained, then hopefully communication will be enhanced, not only while the patient is participating in the individual trial but during future interaction with her physician, nurse and the rest of her treatment team.

201 INVITED

Influence of the Internet and information on the doctor/patient relationship

Abstract not received.

Thursday, 21 March 2002 16:30–18:00

PROFFERED PAPERS

Adjuvant therapy

202 ORAL

The ATAC ('Arimidex', Tamoxifen, Alone or in Combination) adjuvant breast cancer trial in postmenopausal (PM) women

J.S. Tobias. *UCL Medical School, the ATAC Trialists' Group, London, UK*

Anastrozole (A) is superior to tamoxifen (T) in treatment of postmenopausal (PM) women with early breast cancer (EBC) * first results of the ATAC ("Arimidex", Tamoxifen, Alone or in Combination) trial

Introduction: The ATAC trial evaluated, in a randomized, double-blind design, "Arimidex" (A, 1mg), alone or in combination with T (C), relative to T (20 mg) alone as adjuvant treatment for PM patients (pts) with EBC.

Methods: Pts with operable invasive breast cancer (BC) who had completed primary therapy and were eligible to receive adjuvant hormonal therapy were included. Main endpoints (E) were disease-free survival (DFS) and tolerability. Other E included incidence of contralateral (CL) BC.

Results: 9366 pts were recruited (N=3125, 3116, and 3125 for A, T, and C, respectively). Median duration of therapy was 30.7 mth and median follow-up was 33.3 mth. Total event numbers were 317, 379, and 383 for A, T, and C, respectively. 84% of pts were known to be ER+ and/or PR+. DFS was significantly improved for A vs T (p=0.013). Incidence of CL BC was significantly reduced for A vs T (p=0.007). A was significantly better tolerated than T (endometrial cancer, vaginal bleeding/discharge, ischaemic cerebrovascular events, thromboembolic events, hot flushes and weight gain) ($p<0.03$ for all). T was significantly better tolerated than A (musculoskeletal disorders and fractures) ($p<0.03$ for both).

Endpoint	Comparison	HR*	95.2% CI	p-value
DFS (all pts)	A vs T	0.83	0.71* 0.96	0.013
	C vs T	1.02	0.88* 1.18	0.8
OR** 95% CI p-value				
CL BC (all pts)	A vs T	0.42	0.22* 0.79	0.007
	C vs T	0.84	0.51* 1.40	0.5

* hazard ratio; ** odds ratio

Conclusion: A showed superior efficacy to T for DFS and CL BC. These early findings show A as an effective and well tolerated endocrine option for the treatment of PM pts with EBC. Longer follow-up and long-term data on bone mineral density and cognitive function are required to allow a complete benefit / risk assessment to be made.

203 ORAL

Effect of filgrastim on dose intensity of adjuvant CMF with concomitant radiotherapy in patients with operable breast cancer. A prospective randomized study

R. Paridaens[1], J. Wildiers[1], H. Dumez[1], C. Weltens[1], W. Van den Bogaert[1], E. Van Limbergen[1], R. Aerts[1], V. Bormans[2], M. Dauwe[2], A.T. van Oosterom[1]. *[1] University Hospital Gasthuisberg, Medical Oncology, Leuven, Belgium; [2] Amgen, Belgium,*

Objectives: We showed previously that patients (pts) receiving concomitant radiotherapy (RT) and adjuvant CMF were at high risk of neutropenic events compromising the achievement of optimal dose delivery. The main goal of this randomized trial is to investigate the ability of filgrastim (r-metHuG-CSF, Neupogen®) to ameliorate total dose delivery and dose-intensity of adjuvant CMF in combination with radiotherapy (RTCT). The effect of filgrastim support on overall and haematological tolerance, haematological parameters at one year after surgery and cutaneous and pulmonary tolerance on RT was also evaluated.

Methods: A cohort of 102 pts with operable invasive breast cancer having completed surgery and initiating adjuvant chemotherapy (CT) with CMF (600/40/600 mg/m* IV, d1&8, q 4w, 6 cycles planned) concomitantly with radiotherapy were registered. At first event affecting dose intensity (ANC $<$ 1500 imposing delay on d1, or reduction on d8 of any cycle), pts were randomized to pursue their CT either with further support with filgrastim.5 μg/kg sc daily, given on days 2 to 6 and 9 to 13 of each remaining cycle (Group A) or without filgrastim, unless for eventual treatment of febrile neutropenia (Group B). The main endpoint was to compare the proportion of

pts receiving at least 90% of the planned CT, as measured by relative total dose intensity (dose/time: RTDI) and program-RTDI (RTDI times proportion of cycles received/planned).

Results: Among the 102 pts registered, 46 presented a neutropenic event, of whom 9 refused consent to be randomized. Baseline characteristics of the 37 randomized pts include a mean age of 47y (range 31-67), most being premenopausal (78%) with positive axillary nodes (54%) and having undergone breast conserving surgery (68%).

The proportion of pts achieving a mean RTDI > 90% in Group A (19pts) was significantly higher than in Group B (18pts): 52,6% vs 16,7%, P=0.04. The mean program RTDI was also higher in Group A (47,4% vs 16,7%), the difference being of borderline significance (P=0.08).

In group A 47.4% of pts had any adverse event vs 66.7% in group B during CT. A comparison focusing on haematological toxicities during CT (worst cycle, grade III-IV) showed no significant differences in Hb, WBC, ANC or platelet levels between groups A and B. Late sequelae one year after surgery were rare and comparable in both groups.

Conclusions: Filgrastim has a positive effect on chemotherapy dose delivery in patients treated with CMF started concomitantly with RT. Although under filgrastim a higher dose-intensity could be achieved, there were no significant differences between the two groups concerning haematological toxicity and overall tolerance during CT nor for late sequelae at one year after surgery.

204 ORAL

Neutropenia with adjuvant CMF: Is it a marker of effective dosing?

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We have audited the treatment at our institution of 750 women with early breast cancer, given post-operative adjuvant i.v. CMF between 1984 & 1998. The regimen consisted of 750 mg/m2 cyclophosphamide, 50 mg/m2 methotrexate and 600 mg/m2 5-Fluorouracil once every 3 weeks for 6 cycles, followed by tamoxifen 20 mg daily for 5 years in those with ER+ve tumours.

Results ñ Patients: Due to changing treatment policies, more than 50% of the patients were treated during the last 3 years of the period. Median age was 48 years, range 24 ñ 76 years. 70% of patients were pre-menopausal, and 13% were aged over 60 years.

505 patients (67%) had stage II disease, 68% had involved lymph nodes, 55% had grade III tumours. 174 (23%) were ER negative.

Results ñ Treatment: 93% of patients completed all 6 courses. 51% had a treatment delay, and 9% a dose reduction due to toxicity. Neutropenia grades 2, 3 or 4 occurred in 18%, 28% and 10% respectively, and occurred more commonly in older patients ($p < 0.01$). Median received dose intensity was 69%, range 44%–114%.

Results ñ Outcome: There were two suspected treatment related deaths and 11 non cancer deaths. Overall 5, 10 & 15 year cause specific survivals were 71%, 63% and 54% respectively, with the number of involved axillary nodes being the strongest predictor of outcome. Patients who completed less than 4 cycles of chemotherapy had a poorer outcome (51% vs 73%, $p = 0.005$), but there was no difference in outcome according to received dose intensity. However those patients who had a maximum of grade 2 or 3 neutropenia did significantly better (82% vs 64% @ 5 years, $p = 0.0003$) as compared with those who had either neutropenia grades 0, 1 or 4. This was independent of the year of treatment, age of patient, ER status, number of involved axillary nodes and tumour grade. In multivariate analysis, grade 2 & 3 neutropenia remained an independent prognostic factor along with axillary nodal status and ER status.

Conclusion: These data indicate that a lack of neutropenia is associated with a poorer outcome, suggesting that neutropenia could be an effective marker of individual patient pharmacokinetics and hence anti-tumour dynamics.

205 ORAL

Peripheral blood count nadirs during adjuvant CMF chemotherapy for breast cancer - lack of prognostic relevance

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Chemotherapy induced leucopenia was reported to predict favourable survival in various tumors including breast cancer. We analyzed prognostic impact of nadir values of white blood count (WBC), red blood count (RBC), haemoglobin (HGB) and platelets (PLT) in a group of 236 consecutive operable breast cancer patients treated with adjuvant CMF chemotherapy between 1990 and 1995.

Median age in analyzed group was 46 years, proportion of respective clinical TMN categories was as follows: T1 - 21%, T2 - 71%, T3 - 6%, T4 - 1%; N0 - 54%, N1 - 43%, N2 - 3% of cases. Histological diagnosis included ductal (85%), lobular (14%) and other types (1%) of adenocarcinoma. All patients received chemotherapy according to CMF schedule (94% - oral cyclophosphamide; 6% - i.v. cyclophosphamide). 89% of patients completed 6 courses of treatment. Postoperative radiotherapy and hormonotherapy were given in 17% and 12% of patients respectively.

Univariate and multivariate survival analysis was performed with log-rank test and Cox proportional hazards model with use of Wald's statistics to test each variable in backward stepwise regression.

Actuarial survival probability at 5 and 10 years was 78% and 63%, respectively. In the univariate analysis of overall and relapse-free survival, neither WBC nadir value during chemotherapy (p=0.63 and 0.61, respectively), RBC (p=0.17 and 0.13), HGB (0.85 and 0.44) nor PLT (p=0.31 and 0.41) influencd prognosis. The impact of other clinical factors in multivariate model will be presented during the conference.

In our series, nadir peripheral blood counts during adjuvant chemotherapy for breast cancer did not carry prognostic information for overall or relapse free survival.

206 ORAL

The NCIC CTG MA.14 experience with the gallbladder toxicity of octreotide pamoate (oncolar) in a postmenopausal patient population undergoing adjuvant treatment for stage 1-3 breast cancer

M. Pollak, K. Pritchard, T. Whelan, D. Bowman, S. O'Reilly, M. Burnell, L. Shepherd, P. Richardson, D. Tu. *National Cancer Institute of Canada Clinical Trials, Queen's University, Kingston, Canada*

In August 1996, a randomised trial of Antiestrogen Therapy vs Combined Antiestrogen and Octreotide Therapy in post menopausal women was activated to determine the clinical relevance of the laboratory observation that somatostatin analogues enhance the efficacy of tamoxifen (T). Patients were allocated to T 20 mg daily or Octreotide (O) plus T (OT) 90 mg by depot injection monthly for 5 years. Adjuvant chemotherapy was optional. Gallbladder (GB) ultrasounds (U/S) were requested at baseline unless patients had undergone cholecystectomy, and at treatment completion or discontinuation of therapy. Toxicity was monitored at regular intervals. In 1999, after a review of the cumulative risk of cholecystectomy in women with normal baseline U/S, a rate of approximately 6% was noted with 2 years of OT therapy. GB symptoms were reported at 5.3% on OT vs 1.3% on T. Based on a projected risk of cholecystectomy increasing to 16.3% at 30 months, duration of O was decreased to 2 years with T continuing for 5 years. The sample size was decreased from 850 to 650 allowing the detection of a hazard ratio of 1.5 with 80% power. The study closed in July 2000 with 667 patients accrued. Current cumulative risk for cholecystectomy after 2 and 3 years of OT is 2.2% and 8.9% with 47 patients still on OT. Interestingly, the NSABP conducted a trial of similar design, B29, and noted an alarming incidence of GB symptoms. Cholecystectomies reported on the OT arm were 17.7% vs 1.6% on T (ASCO 2001). The trial was closed due to this unexpected risk. Possible reasons for the different toxicity observed in the two trials include a substantially higher mean age of MA14 patients, differing rates of concomitant chemotherapy, and differing thresholds for surgical intervention. Biliary symptoms and other toxicity, cholecystectomy rates, and aspects of quality of life will be presented. The toxicology observed to date on the OT arm would be acceptable if a clinically significant difference in efficacy between arms was observed in this moderate risk population.

Supported by Novartis Pharmaceuticals Canada Inc.

207 ORAL

Body size, received dose-intensity and myelotoxicity of adjuvant chemotherapy in relation to outcome of premenopausal women with N1 breast cancer: results from a National Cancer Institute of Canada randomized controlled trial

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Background: Obesity (body mass index = BMI*25kg/m2) has an adverse impact on outcome in women with early stage breast cancer (BC), but it is common to limit chemotherapy dose in very large patients (pts), leading to diminished received dose-intensity (RDI) and myelotoxicity (MT)- both proposed surrogate markers of outcome. We hypothesized that: (1) obese pts would have a worse outcome than leaner pts, independent of RDI, (2) pts with lower RDI would have a worse outcome, (3) pts experiencing significant MT would have better outcome. The study database (JCO 16(8):2651-58, 1998) contains height, weight, clinical variables, RDI and toxicity, allowing exploration of these hypotheses. From12/89-07/93, 716 pre/perimenopausal pts with N+ BC were randomized to six cycles of adjuvant CMF or CEF. Ideal body weight (IBW) was used for BSA calculation if actual body weight (ABW) exceeded IBW by *20kg.

Results: Of 710 eligible pts, 130 were dosed on IBW (all obese) and 580 on ABW. Mean BSA and BMI were 1.73m2 and 26.38kg/m2 respectively. Obesity was prevalent (51.5%), and equally distributed within prognostic subgroups. In multivariate analyses adjusted for known prognostic factors, initial BMI (quadratic variable) was an independent predictor of RFS and OS, p=0.023 and 0.031 respectively. A concave relationship was seen between BMI and outcome, most favorable for BMI 30.0-35.4kg/m2. RFS and OS rates did not differ if ABW or IBW was used for BSA calculation, in any pt group, all p>0.1. The proportion of pts experiencing significant MT decreased with increasing BMI overall, but increased with increasing BMI in those dosed by ABW. MT was highest in pts dosed on ABW, overall and in the obese subgroup. RDI was highest in pts dosed by IBW, overall and in the obese subgroup. The proportion of pts receiving full RDI (>85% of intended) increased with increasing BMI, overall and in those dosed by ABW. Outcome analysis based on RDI was restricted to those dosed by ABW and was in the opposite direction to expected. Outcome analysis based on MT for the same group revealed a trend to improved RFS and OS in those experiencing MT.

Conclusions: We confirm the influence of body size on BC outcome. This effect appears to be independent of RDI, MT, and whether IBW or ABW is used for BSA calculation. The relationship between body size, MT, RDI and outcome is complex and remains under study.

208 POSTER

Tables of anticipated benefit from adjuvant therapy for the individual

R.W. Blamey, D.A.L. Morgan, M. Mitchell. *Nottingham City Hospital, UK*

The relative survival benefits from adjuvant systemic hormonal (HT) and cytotoxic (CT) therapies are well established, by meta-analyses of the Early Breast Cancer Trialists Group. In advising the individual, benefit is best expressed as absolute (AB).

To estimate AB the relative reduction from therapy is applied to the patient's expected chance of death without therapy using the Nottingham Prognostic Index (NPI).

For example (Table) age 45, the AB at 10 years from chemotherapy (PCT), expressed both as number extra alive (or) as women-years (w-y) gained:

NPI group	No PCT	PCT	w-y gained by 10 yrs	
	10 yr OS%	10 yr extra alive %	Total from all 100	Average per women treated
Excel (EPG)	91	1	5	0.05
Good (GPG)	81	3	15	0.1
Mod (MPGI)	71	5	25	0.3
Mod (MPGII)	59	8	40	0.4
Poor (PPG)	39	11	55	0.6
V Poor (VPG)	18	16	80	0.8

Tables will be presented for hormone therapy (ER+) and CT, at ages 45, 55 and 65 for clinical use.

209 POSTER

Pattern of hormone receptor status of secondary contralateral breast cancers in patients treated with adjuvant tamoxifen

T. Bachleitner-Hofmann[1], B. Pichler-Gebhard[1], M. Rudas[2], M. Gnant[1], S. Taucher[1], D. Kandioler[1], P. Dubsky[1], S. Roka[1], E. Sporn[1], R. Jakesz[1]. [1] *University of Vienna, Department of Surgery, Vienna, Austria;* [2] *University of Vienna, Department of Pathology, Vienna, Austria*

Introduction: Patients with breast cancer receiving adjuvant tamoxifen have a 30% reduced risk of developing contralateral breast cancer (CBC) than patients never treated with the drug. As an antiestrogen, tamoxifen predominantly controls the growth of estrogen receptor (ER)-positive tumor cells. We have evaluated whether CBCs arising in patients treated with adjuvant tamoxifen preferentially display an ER-negative phenotype, in order to gain more insight into the mechanism of prevention of tamoxifen in breast cancer treatment.

Methods: The present retrospective analysis comprises 35 patients with breast cancer (median age 65 years, range 39-86 years) treated with adjuvant tamoxifen at our institution who developed a CBC during the follow-up. The ER and progesterone receptor (PgR) status of both the primary and the contralateral cancers was determined using immunohistochemistry.

Results: Of 35 primary breast cancers, 25 were ER-positive (10 PgR-positive, 15 PgR-negative) and 10 were ER-negative (8 PgR-positive, 2 PgR-negative). The median interval between the primary tumor and the CBC was 34 months (range 8 to 144 months). 5 out of 10 patients with an ER-negative primary tumor again developed an ER-negative CBC (PgR-negative in all cases), in other 5 patients an ER-positive CBC was diagnosed (PgR-positive in all cases). 3 out of 25 patients (12%) with an ER-positive primary breast cancer developed an ER-negative CBC (PgR-negative in all cases), whereas the remaining 22 patients (88%) again developed an ER-positive CBC (PgR-positive in 15 cases, PgR-negative in 7 cases). ER-positive CBCs occurred after a median interval of 37 months (range 10-144 months), whereas ER-negative tumors occurred after a median interval of 25 months (range 8-120 months).

Conclusions: 27 of 35 (77%) CBCs during or following tamoxifen treatment were ER-positive, only 8 of 35 (23%) contralateral cancers were ER-negative. Interestingly, when comparing the primary and contralateral cancers, the percentage of ER-positive tumors increased slightly from 71% (25 of 35 primary cancers) to 77% (27 of 35 CBCs). Contrary to our expectations, our data indicate that adjuvant treatment with tamoxifen does not lead to a selection of ER-negative CBCs. The fact that ER-negative CBCs tended to occur earlier than ER-positive cancers seems to indicate a somewhat more aggressive course of ER-negative as compared to ER-positive tumors.

210 POSTER

8 weeks dose-dense adriamycin/docetaxel (ADOC) versus 24 weeks standard ac followed by docetaxel as preoperative chemotherapy (cht) in operable breast cancer (t2-3, n0-2,m0) - an interim analysis of the Geparduo-study

S. Costa[1], G. von Minckwitz[1], G. Raab[2], M. Schütte[3], J. Blohmer[4], A. Caputo[5], M. Kaufmann[1]. [1] *Goethe - University, Obstetrics and Gynecology, Frankfurt/Main, Germany;* [2] *Bavarian Red Cross Hospital, Obstetrics and Gynecology, Munich, Germany;* [3] *Bethesda Hospital, Obstetrics and Gynecology, Essen, Germany;* [4] *Charite Humbold University, Gynecology, Berlin, Germany;* [5] *Albert-Ludwigs University, Biometrics and Statistics, Freiburg, Germany*

In a previous phase II b -trial including 248 patients (Pts) we have demonstrated that preoperative dose-dense ADOC (adriamycin 50mg/m2 + docetaxel 75 mg/m2 q 14d x 4 + G-CSF + Tamoxifen) results in a pathological complete response (pCR) - rate of 9.7% (von Minckwitz et al., J Clin Oncol 2001). In the present study pts. with cT2-3, cN0-2,M0 untreated breast cancer were randomized to receive either ADOC or AC-DOC (adriamycin 60 mg/m2 + cyclophosphamide 600 mg/m2 q 21d x 4 followed by docetaxel 100 mg/m2 q21d x 4). Primary aim of the study was to demonstrate equivalence of both study schedules in terms of pCR. Tamoxifen (20 mg/d for 5 years.) was given simultaneously in all P.

Within 27 months 913 pts. of 1000 planned have entered this trial. Median age was 51 years; median initial tumour diameter by palpation and by best appropriate imaging method was 4 cm; 39% had no palpable axillary lymph nodes. So far data on toxicity are available for 208 pts who completed the therapies. AC-DOC was associated with a higher rate of neutropenia (71.4% vs. 33%), nausea (11.2% vs. 3.9%), skin/nail toxicity (15.5% vs. 6.8%) and neurotoxicity (4.1% vs. 1%). One grade III/IV fluid re-

tention (ADOC) but no cardiac events were observed. Therapy was stopped preterm in 36 P (ADOC 17, AC-DOC 19) because of toxicity (17 pts), progression (4 pts), death (1 pts), other causes (5 pts), and for lack of compliance (9 pts). Overall breast conservation rate was 75.8%. In 56 of 378 pts. (14.8%) a pCR with no detectable viable and/or in situ tumor cells was achieved. Interim analysis on 378 pts. has revealed an extensive difference in pCR -rate between both study arms. The recruitment was stopped according to the DMC recommendation.

Conclusion: Dose dense and sequential adriamycin/docetaxel regimens have acceptable toxicities but show a considerable difference in efficacy.

211 POSTER

Weight change in premenopausal breast cancer (BC) women at ≥12 months after diagnosis

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Introduction: Weight change in patients with BC is widely observed, but poorly described clinical problem. The study is aimed at estimating the frequency and risk factors for weight change at least 1 year after primary diagnosis of BC.

Material and Methods: Weight was measured in 189 premenopausal BC women (median age: 37 yrs, range: 32–53) at diagnosis and ≥12 months afterwards (range: 12–19, median: 14.5). All patients were primary mastectomized and 72% of them (N = 136) have received adjuvant therapy (chemotherapy - 93, chemotherapy and tamoxifen 43, locoregional radiotherapy - 87), while 28% (N = 53) were assigned to observation. All study participants were clinically free of disease during analysis period.

Results: The median weight change in the study group was +2.7 kg (range: −3.0–+17.2 kg). Treated women gained significantly more weight than patients in observed population (7.1 vs. 1.9 kg, respectively; $p < 0.001$). Weight gain of at least 1.0 kg was noticed in 67% (N = 127) patients and was significantly more frequent in treated women as compared to the observation group (74% vs. 47%; $p < 0.01$). In patients who received adjuvant therapy, the prevalence and magnitude of weight gain were not associated with estrogen receptor status, primary tumor size, axillary lymph nodes status, inclusion of radiotherapy or duration of tamoxifen administration. Weight gain of ≥1 kg occurred more frequently in initially obese women as compared to those with normal weight ($p < 0.002$), patients treated with tamoxifen ($p < 0.05$) and CMF regimen as compared to anthracycline-containing chemotherapy ($p < 0.01$) as well as in those who developed amenorrhea ($p < 0.003$).

Conclusion: Our data confirmed that weight gain is observed in the great majority of BC women receiving adjuvant therapy and suggest that risk factors for it may include treatment with tamoxifen and CMF regimen, initial obesity and induction of amenorrhea with chemotherapy.

212 POSTER

Acute and late toxicity following adjuvant high-dose chemotherapy for high-risk primary operable breast cancer

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Background: Patients with node-positive breast cancer are at greater risk for relapse compared to node-negative patients. To improve outcome, high-dose chemotherapy with haematopoietic stem cell support was employed from 1996 to 2000 at Herlev Hospital as an adjuvant treatment strategy for management of primary high-risk breast cancer patients with more than five positive nodes. As available data indicate at most a marginal benefit of high-dose therapy we find it relevant more thoroughly to document the morbidity, as well as the requirement of supportive therapy associated with high-dose treatment.

Study: This single institution study included 52 women aged * 56 years with primary operable breast cancer and more than 6 tumour-positive axillary lymph nodes. The treatment regimen consisted of at least three initial courses of FEC (5-Fluorouracil 500 mg/m2, Epirubicin 90 mg/m2, Cyclophosphamide 500 mg/m2) followed by high-dose chemotherapy (Cyclophosphamide, Thiotepa, Carboplatin, STAMP-V) supported by autologous peripheral blood stem cell reinfusion. Furthermore, patients received radiotherapy (2 Gy x 24). Data regarding organ toxicity were processed for evaluation of short and long-term side effects associated with the treatment regimen.

Results: No treatment related death occurred. There was substantial acute toxicity including frequent catheter-related infections. Long-term toxicities included reduced lung diffusion capacity (n=36), fatigue(n=14), arthralgia/myalgia (n=10), neurotoxicity (n=9) and memory loss (n=4). However, most toxicities were grade 1-2 and reversible within two years. The majority of patients regained working ability after one year. Quality assessment of the stem cell graft revealed cytokeratin 19 positive tumor cells in 3 of 37 tested patients (8%). Within a median follow-up of 30 months (range, 11-57), 25% of the patients had relapsed. Recurrence free survival was 75% and overall survival was 88% three years after treatment start.

Conclusion: Our main objectives were to assess toxicity and the applicability of the HDC strategy. Apart from two isolated cases of severe renal and pulmonary toxicity the high-dose treatment was relatively well-tolerated without serious organ toxicity and without toxic deaths. Thus, the treatment was found to be feasible with manageable toxicity and an acceptable requirement of supportive therapy.

Thursday, 21 March 2002 16:30–18:00

PROFFERED PAPERS

Targeted therapies

213 ORAL

Safety of Herceptin monotherapy administered on a 3-weekly schedule: preliminary data from a phase II study in women with HER2-positive metastatic breast cancer

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Background: The standard weekly dosing regimen of Herceptin, alone or with paclitaxel, is well tolerated and efficacious. However, less frequent dosing would be more convenient and also logical, in view of the long terminal half-life of Herceptin (28.5 days). A 3-weekly schedule of Herceptin has been shown to be well tolerated in combination with 3-weekly paclitaxel. This study examines the same 3-weekly schedule of Herceptin given as monotherapy.

Methods: Women with previously untreated HER2-positive (IHC 3+ or FISH positive) metastatic breast cancer and left ventricular ejection function (LVEF) >50% were eligible. All patients were treated with Herceptin 8mg/kg i.v. loading dose, followed by 6mg/kg every 3 weeks. The primary objective is response rate, with time to progression, rate of symptomatic heart failure and serious infusion reactions, and pharmacokinetics (PK) as secondary objectives.

Results: At the time of reporting, 91 patients had entered the study. One patient did not receive Herceptin and is excluded. Mean patient age was 53 (23-84) years; 43% of patients had lung and 38% had liver metastases; 71% had received prior adjuvant chemotherapy; 46% had received anthracyclines. 71 patients were known to have centrally confirmed HER2-positive disease (IHC 3+, FISH positive or both). Patients had received a median of 4 (1-13) cycles of 3-weekly Herceptin and 45 patients had discontinued therapy (42 due to progressive disease/insufficient therapeutic response, 2 due to death and 1 due to an adverse event). Therapy has been well tolerated, with most side effects mild to moderate in severity. No unexpected adverse events were encountered. Only 17 NCI-CTC grade 3 and two grade 4 events (cerebrovascular accident and cardiac tamponade, both unrelated to Herceptin) have occurred. Baseline LVEF was 63% (49-84%) and no patient has developed symptomatic cardiac failure. Preliminary data have shown that patients with very high ECD concentrations at baseline have correspondingly low serum concentrations of Herceptin. Further PK and preliminary efficacy data will be presented.

Conclusions: Administration of Herceptin every 3 weeks, at 3 times the standard dose, is a well-tolerated alternative dosing regimen that merits further investigation.