reliably assess the optimal duration of TAM must be large with long follow-up if any worthwhile benefit is to be detected. So, results of small trials of 5 versus 10 years of TAM are conflicting with some studies, perhaps wrongly, suggesting that 5 years is sufficient.

ATLAS is an international randomised trial of longer versus shorter hormonal therapy. It aims to assess reliably the effects of prolonging TAM by an extra 5 years in women who have already had some years of treatment and for whom there is uncertainty as to whether they should stop now. 10–20,000 women will be randomised, usually after 5 years of TAM, to either stop, or continue TAM for 5 more years. This large, simple trial is designed to integrate into routine clinical practice with almost no documentation; since the main analysis will be of all-cause mortality. ATLAS will also provide information on both cause-specific mortality and non-fatal, but important events. If, by 2020, ATLAS shows improved long-term survival with 10 years of TAM (e.g. 27.5% vs. 30% dead), this result will save thousands of lives annually, and will be relevant to the appropriate use of hormonal therapies in general.

178 POSTER

Dose-dense weekly docetaxel and CBDCA in adriamycin-resistant metastatic breast cancer (MBC)

Mehrdad Salimi, M.R. Mir. *Iranian Cancer Institute, Mehr Hospital, Zartosht Ave. Tehran, Iran*

We have studied 60 Pts. with MBC with the following characteristics: median age 55 (range 30–73) ECOG-PS 0:10 1:38 II:12

Protocol Design: Docetaxel (D) 60 mg/m^2 as one hour infusion followed in one hour by Carboplatin (C) 200 mg/m^2 as 30 min infusion weekly for 6 wks. Median dose intensity (mg/m^2/week, based on 6 wks of treatment and 2 wks rest period): Docetaxel: 42 mg/m^2, Carboplatin 142 mg/m^2. Hematoligical toxicity (WHO-Grading): Hbl:12 (20%); II:8 (13%) III:6 (10%); Leukocytes 21 (35%); II:8 (13%); III:6 (10%); Platelets I:14%; II:6%.

Peripheral Side Effects: Alopecia I:20 (33%), II:30 (50%); Sensory neuropathy I:10 (16%), II:5 (8%), no other side effects other than the above-mentioned observed.

Response Analysis: CR: 15 (25%), PR:33 (55%), NC:7 (11%), PD:5 (8%).

Conclusions: Dose-dens weekly Docetaxel/Carboplatin is active in Adriamycin-resistant MBC. Hematological and peripheral toxicities are not significant. A platelet sparing effect seems to exist with this regimen. Overall treatment time is shortened in comparison with Q.3 WK schedules, whereas dose intensity for Docetaxel is increased. The excellent tolerability recommends weekly D/C for ambulatory treatment.

179 POSTER

Hormonotherapy with goserelin depot after adjuvant chemotherapy in premenopausal women with early breast cancer: Is there any benefit?

A. De Matteis, D. Montedoro, F. Nuzzo, G. Landi, V. Labonia, E. Rossi, G. D'Aiuto. *Istituto Tumori, Naples, Italy*

There is the definite evidence that adjuvant chemotherapy can affect both recurrence and survival with 21% reduction for recurrence and 11% reduction for mortality. Ovarian ablation in women aged under 50 was associated with 6% fewer recurrence and deaths after 15 years. Adding hormonotherapy to chemotherapy theorically could improve results depriving ER+ cells of oestrogen stimulus. In order to evaluate the effectiveness of hormonotherapy with Goserelin depot given soon after adjuvant chemotherapy with Epirubicin (110 mg/sqm) d 1 q 3 weeks × 4 followed by CMF d 1,8 q 4 weeks × 4 cycles, 92 premenopausal patients with ER+ breast cancer were randomly allocated after chemotherapy to stop therapy or to receive Goserelin depot 3.6 mg s.c. q 28 d × 2 years. In our experience the addition of Goserelin depot to sequential chemotherapy Epirubicin and CMF showed no benefit in terms of overall survival and DFS after a median follow-up of 46 months. This is not surprising if we keep in mind that chemotherapy caused amenorrhoea in up to two thirds of our patients during adjuvant treatment. Therefore, adding LHRH analogues may not result in significant additional benefit in the majority of women treated, but we can also hypotize that very large numbers of patients may be required before such a benefit can be seen.

180 POSTER

Second- and third-line treament of metastatic breast cancer with gemcitabine

T. Brodowicz, R. Möslinger, V. Herscovici, I. Vaclavik, C. Wiltschke, E. Kubista, C. Zielinski. [1]*Clinical Division of Oncology;* [2]*Chair of Medical-Experimental Oncology;* [3]*Department of Gynaecology and Obstetrics; University of Vienna, Department of Internal Medicine I, Austria*

In the present study, 24 female breast cancer patients with visceral metastases were treated with intravenous gemcitabine 1250 mg/m2 on days 1, 8, and 15, q28d. In 6 patients gemcitabine was administered as second-line chemotherapy, whereas 18 patients received gemcitabine as third-line chemotherapy with previous chemotherapeutic regimens containing an anthracycline in all patients and taxanes in 8 patients.

2 (33%) of the 6 patients receiving gemcitabine as second-line chemotherapy showed a PR, and 4 patients (67%) developed SD. The median overall survival was 15.1 ± 6.7 months (range: 11.4–27.3), the median time to progression was 12 ± 3.4 months (range: 5.6–15.1). In the third-line setting, 1 (6%) out of 18 patients gained CR, 6 (33%) SD and 11 (61%) PD with a median overall survival of 6.3 ± 5.9 months (range: 2.4–23.8) and a median time to progression of 3.9 ± 1.7 months (range: 1.5–8) ($p < 0.01$).

Treatment-related toxicity in the two subgroups was similar. Second-line: anemia WHO grade I or II occurred in 3 (50%) patients; leukopenia grade I or II in 2 (34%), grade III in 4 (67%) patients; thrombopenia grade I or II in 4 (66%) patients, grade IV in 1 (17%) patient. In patients receiving gemcitabine as third-line therapy, 11 (61%) patients developed anemia WHO grade I or II, 2 (11%) patients anemia grade III. Leukopenia grade I or II was observed in 10 (55%) patients, grade III or IV in 4 (23%) patients. Thrombopenia grade I or II occurred in 9 (50%), grade III in 3 (17%) patients.

We thus conclude that gemcitabine was an effective therapy in patients with advanced breast cancer after previous chemotherapeutic agents including anthracyclines and taxanes. When administered early, gemcitabine led to a prolonged interval until progression occurred.

181 POSTER

Mitomycin (M), epirubicin (E) and vinorelbine (V) first-line chemotherapy for metastatic breast cancer (MBC). A feasibility study

Alessandro Neri, Alfredo Guarnieri, Enrico Tucci[1], Fiorella Pepi[1], Bruno Mazzocchi[2], Renato Algeri[2]. *Inst. of Surgical Sciences;* [1]*Dept. Radiotherapy, Univ. of Siena* [2]*Medical Oncology, Grosseto Hospital, Italy*

In our experience the combination of M and E showed high activity and good tolerability in MBC (Pacini P., EJC, 1994), with a response rate of 70%. The addition of V to E and M could improve these results without compromising tolerability. In order to evaluate the feasibility and compliance of MEV combination, a pilot study started on June 1996. Treatment schedule was: E 75 mg/sqm and M 10 mg/sqm on d. 1; E 75 mg/sqm and V 25 mg/sqm on d. 21; V 25 mg/sqm on d. 28 (1 cycle). Cycles were repeated every 3 weeks. G-CSF administration was planned according to the hematologic toxicity observed during the treatment. So far 16 patients (pts) were enrolled. Median age was 56 ys (37–70), median PS was 1 (0–3); all pts had visceral metastases. No pt was excluded from evaluation for response and toxicity. Patients received a median of 3 cycles (2–4). We observed 2 CR, 9 PR, 5 NC, no pts showed disease progression. As for toxicity, alopecia was universal, granulocytopenia grade 3–4 occurred in 8 pts, no other grade 4 toxicity was recorded; G-CSF was administered to 7 pts. On conclusion, MEV is a safe and probably very active chemotherapy for MBC as outpatients. Accrual of pts is ongoing in oredr to fully assess activity in a large series.

182 POSTER

Sequential or simultaneous chemo-radiotherapy in operable breast cancer. A French multicentric phase III study – State of inclusions

C. Noguès[1], J.-R. Garbay[1], D. Serin[2], Y. Graïc[3], B. Leduc[4], L. Demange[5], V. Lucas[6], M. Combe[7], D. Castera[8], J. Rouëssé[1]. *Co-invest;* [1]*Centre René-Huguenin, Saint-Cloud;* [2]*Clinique Sainte-Catherine, Avignon;* [3]*Centre Henri Becquerel, Rouen;* [4]*Centre Haspitalier de Brive;* [5]*Institut Jean Godinot, Reims;* [6]*Hôpital de la Source, Orléans;* [7]*Centre Hospitalier Le Mans;* [8]*Clinique Saint-Pierre, Perpignan, France*

Purpose: We compare two adjuvant modalities in operable breast cancer patients. After initial surgery (tumorectomy or mastectomy) with axillary

N+ status (1 to 7 positive nodes), patients are randomised between FNC and simultaneous locoregional radiotherapy (arm A) or FEC (Epirubicin 60 mg/m^2) followed by radiotherapy (arm B). After age 50, recommended attitude of hormonotherapy is to given tamoxifen 20 mg daily, whatever the tumor hormonal status.

Methods: Primary end point is 5 years Disease Free Survival (DFS). Secondary objectives are loco-regional recurrence, immediate and late toxicity and quality of life (EORTC QLQ-C30). To show 0.10 discrepancy between 5 years DFS (0.65 vs 0.75), 650 patients are required ($\alpha = 0.05$, 2 sided, $\beta = 0.20$). Stratified randomisation is done according to the center (11 centers), the number of positive nodes (1–3/4–7) and the type of surgery (tumorectomy/mastectomy). No interim analysis is planned.

Results: This trial began in December 1994 and is still going on, involving 502 patients up to January 98 (251/251). The inclusions will be closed at the end of 1998. Tumorectomy is realised for 2/3 of the patients and the number of nodes involved is 1–3 for 80% of them. There is no imbalance between the two arms in term of clinical and histologic factors. The patients follow-up is obtained at 4 months for 80% (A) vs 71% (B), and at one year for 59% (A) vs 53% (B).

183 POSTER

Does the administration of anthracyclines affect human tumour blood flow?

K. Goodchild[1], S. Hill[2], A. Makris[1], D. Chaplin[2]. [1]*Mount Vernon Hospital, Northwood;* [2]*Gray Laboratory Research Trust, Northwood, UK*

Introduction: The use of anthracycline-containing drug regimes is increasing in both the neoadjuvant and adjuvant treatment of breast cancer. Tumour blood flow is an important parameter in treatment outcome. Studies in mice bearing human tumour cell lines have shown that administration of doxorubicin can consistently reduce regional blood flow as measured by laser Doppler flowmetry. Reduced blood flow may compromise the delivery of subsequent drugs reducing the efficacy of treatment or alternatively may potentiate the effects of bioreductive agents such as mitomycin C.

Aim: To investigate the effect of anthracycline administration on human tumour blood flow.

Methods: Six consecutive females undergoing neoadjuvant chemotherapy for primary breast cancer were studied. Patients received either FEC (5-fluorouracil 600 mg/m^2, epirubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2) or MM (methotrexate 35 mg/m^2 and mitoxantrone 11 mg/m^2). Up to 6 laser Doppler microprobes were inserted into the primary tumour mass and blood flow was recorded for 10 minutes pre-and for up to 60 minutes post-epirubicin or mitozantrone administration (and prior to the other drugs).

Results: Blood flow has been analysed in 5 patients. Considerable inter- and intra-tumour variabilty has been seen with no consistent trend demonstrated so far.

Conclusions: This technique can be used to measure human tumour blood flow after administration of chemotherapy. Results from this study may influence patient management by identifying which tumours may benefit from the addition of blood-flow modifying agents to the anthracycline-containing regime.

184 POSTER

Ocular toxicity related to tamoxifen therapy

S. Veselinović, S. Filipović, D. Veselinović, L. Djordjević, Z. Rančić. *Clinic of Oncology, Surgery & Ophtalmology, Yugoslavia*

Previously published cases suggest that tamoxifen has a potential for causing ophthalmologic toxicity, with retinal, corneal, and optic nerve abnormalities. We analyzed 260 postmenopausal women with operable, No, breast cancer and tried to determine the prevalence of ocular toxicity-after tamoxifen therapy. One group (180 subjects) was treated with 10–20 mg tamoxifen daily, and the other (80 subjects) with 20–40 mg. All of them underwent slit lamp anterior segment examination and fundal examination with direct ophthalmoscopy.

In the 1st, there were 2 cases of central (muscular) retinopathy (total tamoxifen dose 32.4 g and 39.8 g). In the 2nd group, there was 1 patient with corneal opacities, 1 with macular oedema, 1 with optic neuritis. Cumulative doses for the 3 were 29.8 g, 37.6 g, and 42.3 g, respectively.

Both conventional and high dose tamoxifen can cause ophthalmologic complications, as shown in the study, requiring regular ophthalmologic examinations for those on long term tamoxifen.

Thursday, 1 October 1998 16:00-18:00

PARALLEL SESSION

Surgery

188 INVITED

Breast cancer patients treated without axillary surgery: Clinical implications and biological analysis

M. Greco. *Istituto Nazionale Tumori, Milan, Italy*

Until now axillary dissection has been considered an integral part of breast cancer treatment. However, we believe that axillary surgery can be avoided in selected breast cancer patients. 401 breast cancer patients (mean age 62.9 years) underwent breast surgery without axillary dissection from January 1986 to June 1994, principally considering age, and small tumour size. No patients had clinically involved nodes in homolateral axilla. 216 out of 401 patients (53.6%) had a pathological tumour diameter ≤1 cm, 133 (33.6%) were between 1 and 2 cm, whereas 38 (9.5%) had a tumour size >2 cm. The histological diagnosis was ductal infiltrating carcinoma in 188 cases (46.9%), associated to DCIS in 73 cases (18.2%). LIC was present only as histotype in 59 cases (14.7%). Breast conservative surgery was performed in 383 patients (95.6%) and only 18 patients (4.4%) underwent total mastectomy in consideration of the presence of extensive intraductal component. 257 patients (64.1%) received radiotherapy to the operated breast. In elderly patients an adjuvant hormonotherapy was preferred considering the hormonal receptorial status.

An accurate updated follow-up >36 months was obtained in all patients (mean 58.5 months, range 36–122); 58 patients died, 32 for uncorrelated or unknown causes. 29 (7.2%) patients had distant metastases only and 6 (1.5%) patients had axillary and distant metastases syncronally. 28 (6.9%) patients had clinically axillary metastases as only and first site of metastatic disease: 28 patients underwent full axillary dissection showing pathological metastases in 21 cases. The mean number of metastatic nodes was 6 (1–32) and the mean diameter of the primary tumour in these metastatic cases was 16.8 mm. Only one case had a tumour diameter <1 cm. The mean time of disease free interval was 29.1 months. 3 patients out of 34 were treated with radiotherapy to the axilla without surgery, and 3 patients were treated with hormonotherapy. 17 out of 28 operated patients are disease free. Considering the present results, some pathologic, biologic and clinical parameters were retrospectively investigated on the primary tumours of this series, in order to identify an alternative criteria, excluding the nodal involvement, for giving an adjuvant treatment. The results allow to recognize a biological subpopulation of tumours with high risk of distant relapse, indipendently from the axillary nodal status. This study is not a prospective randomized trial, however we can conclude that avoiding axillary dissection does not impair local control of disease and does not have a negative impact on long term outcome in selected patients. However, the risk could be an undertreament of the patients after the breast cancer surgery, due to the lack of information on the axillary nodes for planning adjuvant treatment. The research of alternative parameters on the primary tumours by which planning adjuvant treatments will give the possibility of a better control of distant relapse also sparing the axillary nodes.

189 ORAL

Preoperative MRI does not influence the amount of breast tissue excised in conservative cancer surgery

M. Douek[1], J. Vaidya[1], T. Davidson[1], S.R. Lakhani[2], M.A. Hall-Craggs[3], M. Baum[1], I. Taylor[1]. *Departments of* [1]*Surgery;* [2]*Histopathology;* [3]*Radiology, University College London Medical School, London W1P 7LD, UK*

Aim: Breast magnetic resonance imaging (MRI) provides accurate information about tumour size and location which correlate closely with histological size. Clinical assessment of tumour size is very variable and often overestimates histological size. We assessed prospectively the impact of MRI information on extent of surgical resection.

Method: 96 patients with breast cancer diagnosed by triple assessment, underwent breast conservation surgery over 1 year. Of these patients 29 underwent pre-operative MRI using a T1-weighted 3D FLASH sequence. MRI images were not used for decision-making on type of surgery but were shown to the operating surgeon pre-operatively to indicate the location of the lesion and its local extent. Clinical information and histological assessment