cycle. Mastectomy was done in responders. The sonographic changes were recorded and correlated with histological changes.

Results: Fourteen cases were evaluated. Nine patients showed response in form of reduction in tumour size, improved tumour margin definition, decreased echogencity of tumour, more homogenous internal echos and reduction of skin oedema.

Conclusions: Sonomammography can be used as a readily available cost effective tool for assessment of tumour response following primary chemotherapy in patients with LABC.

61 POSTER

Activity of chemotherapy based on Navelbine in pre-treated metastatic breast cancer patients

A. Lesuik, T. Khodina, E. Zhavrid. *Department of Chemotherapy, Research Institute of Oncology and Medical Radiology, Minsk, Belarus*

Purpose: To evaluate the activity and hematologic toxicity of Navelbine-based combinations in metastatic breast cancer patients previously treated with one or more line of chemotherapy.

Materials: From March 1996 through January 1997, 34 metastatic breast cancer patients were included in the study. The age ranged from 31 to 73 (mean 47). According to ECOG scale, their performance status was 0–2. All the patients had two-dimension measurable or assessable tumor lesions. The sites of metastases were lymph nodes (16 patients), bones (15), lungs (12), skin (8), breast (7), liver (4), kidney (1). The number of metastatic sites was 1 in 9 (26.5%) patients, 2 in 14 (41.2%) and 3 in 11 (32.3%), metastases in the internals occurring in 50% of the cases (in 17 of 34 patients). Twenty-two of the 34 patients had previously received one line of chemotherapy, 12 patients – two lines. The mean number of previous courses of multidrug chemotherapy for one patient was 5 (range 1 to 8). Get the start of Navelbine treatment all patients had a disease progression.

Methods: Twenty-three patients were administered combination chemotherapy: Navelbine 25 mg/m2 day 1 and 8 plus Doxorubicin 50 mg/m2 day 1, every 21 days. Eleven patients were given Navelbine 39 mg/m2 day 1 and 5 plus 5-Fluorouracil 750 mg/m2 days 1 through 5, every 21 days.

Results: We evaluated 122 courses with Navelbine. Leucopenia occurred in 88 (72.1%) courses, but only in 24 (19.6%) courses it was grade III–IV toxicity. Grade III anemia developed only after 1 (0.8%) course. Grade III thrombocytopenia was observed in none of the patients. Navelbine dose had to be decreased due to hematologic toxicity in 13 (10.7%). No treatment-related fatal outcomes were registered. Partial response occurred in 11 (32.4%) patients. 17 (50.0%) stabilizations of disease and 6 (17.6%) progressions were observed. 9 patients (26.5%) are still alive in follow-up time of 9 to 17 months. The median survival was 9.8 months. The one-year survival rate is 36.9%.

Conclusion: Navelbine-based chemotherapy combinations are satisfactorily tolerated and are moderately active in the 2nd or 3rd lines of metastatic breast cancer therapy.

62 POSTER

Vinorelbine (VNR) + 5-fluorouracil continuous infusion (5-FU c.i.) in pretreated advanced breast cancer – Adria Medica Group

S. Cobelli[1], A. Scanni[1], T. Battelli[2], A. Pisone[2], L. Frontini[3], L. Di Lullo[4], R. Mattioli[5]. *[1]Oncology Dept., Fatebenefratelli and Oftalmico Hospital, Milano; [2]Oncology Dept., Torrette Hospital, Ancona; [3]Oncology Dept., S. Paolo Hospital, Milano; [4]Oncology Dept., Civil Hospital Isernia; [5]Oncology Dept., S. Croce Hospital, Fano, Italy*

The results in terms of objective response in pretreated advanced breast cancer are generally not over 30–40%, and the median duration of the response is about 5 months. From March 1997 we investigated the therapeutic effect and the tolerability of a combination of VNR + 5-FU c.i. as second line in patients with metastatic breast cancer.

The schedule is the following:

5-FU	700 mg/m^2 i.v./day	for 5 days	every 3 weeks
VNR	25 mg/m^2 i.v. bolus	day 1 and 6	every 3 weeks

In December 1997 n.27 patients were enrolled and 19 were valuable. Median age 55 years, 4 pts were premenopausal and 23 postmenopausal. Recettorial state: positive 15 patients, negative 5 and 7 unknown. 14 patients had received prior chemotherapy in adjuvant setting, 23 for advanced disease, 13 for both. The site of metastatic disease were visceral + bone 13, bone 6, visceral and soft tissue 21 pts, WHO PS was 0 in 6 pts, 1 in 18 and 2 in 3 pts. There were 8 PR and 6 SD. The median duration of the response was 5 months. 5 pts progressed on treatment.

Toxicity: Grade 1: leukopoenia in 7 pts and grade 3 in 1 pt. Grade 2: mucositis in 4 pts and grade 3 in 1 pt. Grade 3: diarrhea in 1 pt. Grade 4: vomiting in 1 pt. The study is ongoing.

63 POSTER

Treatment of liver-metastases in patients with breast cancer

W. Jäger, G. Wieland, N. Lang. *Dept Ob/Gyn, University of Erlangen-Nuremberg, Germany*

Purpose: Treatment of liver metastases with anthracyclines or antimetabolites leads to few responses and does probably not prolong survival significantly. Therefore the effectiveness of taxanes was tested in these patients.

Methods: Breast cancer patients with only liver metastases as first side of relapse were treated with 200 mg/m2 taxol as monotherapy or in combination with epirubicine (60 mg/m2) (in the latter combination the dose of taxol was reduced to 175 mg/m2). Response was categorized according to the WHO-criteria.

Results: 18 patients were treated between 1994 and 1996 with 200 mg/m2 taxol. One patient achieved a complete remission (CR), 4 patients a partial remission (PR), giving an overall response rate of 30%. Mean duration of response was 5 months and mean survival was 20 months.

10 patients received the combination chemotherapy since 1996. While only one patient achieved a complete remission, 5 patients had a PR, giving a response rate of 60%. Mean duration of response was 8 months. Mean survival could not be calculated since 6 patients are still alive.

Conclusion: In previous studies mean survival of patients with liver metastases was reported to be in the range of 12 months. Using taxol, 6 of the 14 patients survived more than 24 months and the remaining 14 patients are still living. That could be considered as an improvement. According to the still preliminary data the combination with epirubicine could be even more effective.

64 POSTER

Primary medical treatment of locally advanced disease reveals causes of failure of adjuvant chemotherapy

Ann Johnson. *Breast Study Centre, Mount Vernon Hospital, Northwood, UK*

Hypothesis: The sequestered cell – a cell remote from the circulation at the time of treatment – is a major cause of failure of chemotherapy. The effectiveness of systemic therapy may be improved in tumours that shrink slowly (grades I and II) by protracting the treatment to allow time for revascularization of poorly nourished areas.

Methods: New primary breast cancers were treated by sequential single agent therapy (chemotherapy and hormones). Timing was regulated by the rate of shrinkage of individual tumours. The existence of poorly nourished tissue around the margins of ulcerated tumours was demonstrated by thermographic scanning. Sites of recurrent nodules after early healing of these tumours were compared photographically to the original areas of poor circulation.

Results: Despite improved early local control, nearly all tumours eventually regrew. In ulcerated tumours close correspondence was seen between areas of poor circulation and sites of local recurrence.

Conclusions: The demonstrable failure in ulcerated tumours will be repeated on a microscopic scale in smaller, non-ulcerated tumours. If shrinkage, with accompanying improvement of the local circulation, does not occur during treatment, then systemic therapy is unlikely to succeed. Tumours that shrink slowly will do better if treatment time is extended. However, total extinction is rare and therefore surgery should follow when possible.

65 POSTER

Comparative study of taxol (T) and Cisplatin© versus Taxotere (Tx) and vinorelbine (V) in metastatic breast cancer (MBC). Preliminary results

M.R. Rodríguez, J. García Mata, J.L. Fírvida, M. Salgado. *Dept. of Oncology, H. Sta. Mª Nai, C/Ramón Puga, 56, Ourense, Spain*

Introduction: Taxanes have shown important activity as rescue treatment in metastatic breast cancer refractary to anthracycline therapy. In this trial

we have compared the efficacy and toxicity of two different regimens: T 135 mg/m i.v. by a three hours infusion day 1 plus C 75 mg/m day 2 versus Tx 75 mg/m day 1 plus V 20 mg/m days 1 and 5, every three weeks in patients with MBC previously treated with anthracyclines.

Methods: Fron 1/97 to 1/98, 18 evaluable patients entered his study following the usual inclusion and exclusion criterions.

Results:

	T-C	Tx-V
No of evaluable pts.	10	8
No of cycles	45	44
Neutropenia G4 (%)	2 (20)	5 (62)
Febrile Neutropenia (%)	1 (10)	3 (38)
Thrombocytopenia G4 (%)	0	0
Mucositis G3 (%)	0	2 (25)
Peripheral neuropathy (%)	2 (20)	0
CR/PR/SD/PR	2/3/2/3	2/4/1/1
Response Rate	50%	75%

Conclusion: Preliminary results suggest that Tx-V has better activity but with a higher toxicity respect T-C in MBC.

66 POSTER

Liver metastases from breast cancer – Clinical feature and treatment

N. Masuda[1], E. Yayoi[2], Y. Nakano[3], T. Monden[3], J. Okamura[3]. *[1]Dept. of Surgery II, Osaka University Medical School; [2]Dept. of Surgery, Kaizuka Municipal Hospital; [3]Dept. of Surgery, Osaka Teishin Hospital, Japan*

We had treated 55 patients with liver metastases of breast cancer at the Osaka Teishin Hospital from 1986 to 1997. In this study, the clinical feature and effect of systemic or intra-arterial chemo-endocrine therapy for these patients were reviewed to clarify characteristics of liver metastases and establish optimum therapy.

Of 55 patients, one patient underwent hepatectomy, 25 were treated with systemic chemo-endocrine therapy such as CAF combination chemotherapy [A], and 10 were treated with one shot intra-arterial chemoenbolization through hepatic artery using Epirubicin and Lipiodol [B], and the other 19 were treated with hepatic arterial infusion chemotherapy using Epirubicin every 2 weeks and continuous infusion of 5-FU [C]. All patients in [B] and [C] were followed by oral chemo-endocrine therapy of MPA alone or MPA + 5'DFUR.

The response rate in the group of [B] and [C] were better than in group [A], whereas there was no significant difference in survival time among three groups. Intra-arterial chemotherapy can prevent hepatic death due to uncontrolled liver metastases in 64.0%(16/25) of cases. The toxicity in the group of intra-arterial chemotherapy ([B] + [C]) was limited.

The thoracico-abdominal lymph nodes metastases was observed in 25.5% (14/55) of cases. In these patients, liver metastases were seemed to be occurred through lymphogenic route. In the group of intra-arterial chemotherapy, the survival time of patients without metastases in the thoracico-abdominal lymph nodes was significantly longer than that of patients with metastases (2-year survival rate was 45.4% vs 0.0%, respectively; $p < 0.01$).

This study suggests that intra-arterial chemotherapy combined with MPA should be safe, effective and useful for the advanced breast cancer patients with liver metastases. But, in cases of *lymphogenic* liver metastases, to prolong survival, it should be required to combine intra-arterial chemotherapy with *more* intensive systemic chemo-endocrine therapy.

Wednesday, 30 September 1998 16:00-18:00

PARALLEL SESSION

New drugs

71 INVITED

New drugs in breast cancer

L. Mauriac. *Institut Bergonié, Regional Cancer Center, Bordeaux, France*

Breast cancer treatments have progressively evolved for 20 years. The most fruitful steps have been marked by the appearance of anthracyclines (with new form of administration) and recently, by the impact of taxanes. These non cross-resistant drugs are used as sequential or alternating single-agents, both administered intensively or in combination. Another way of development is the use of high-dose chemotherapy. Many non randomized trials have been published so far with very promising results. But, there are not yet any randomized phase III studies to confirm the real value of high-dose chemotherapy. Besides these classical approaches, new research is moving. Its goal is to block several growth factors of the cancerous cells through their receptors (tyrosine kinase receptors): epidermal growth factor receptor (EGFR), erb-B2 and the fibroblastic growth factor receptors. The most promising approach seems to be the monoclonal antibody against erb-B2 which has shown a synergistic effect (taxanes). Another means concerns the use of angiogenesis inhibitors, which are presently in early development. The same state is noted for matrix metalloproteinase inhibitors. They are proteolytic enzymes involved in matrix degradation, which favors tumor invasiveness and metastasis. The last two investigational pathways concern telomerase activity inhibitors and gene therapy: we can imagine that a down regulation of gene overexpression (erb-B2) could reverse malignant properties of tumor cells. Hormonal compounds have also recently been developed: new pure antiestrogens and aromatase inhibitors of second and third generation. One of them inhibits the aromatase and blocks the degradation of retinoic acid.

72 ORAL

EORTC 10941; Final results of a phase II study of liarozole fumarate in patients with metastatic breast cancer

J. Klijn, A. Hamilton, L. Beex, L. Mauriac, R. Paridaens, J.A. Roy, A. Awada, A. Van Vreckem, P. Palmer[1], M. Piccart. *On behalf of the EORTC-IDBBC (Investigational Drug Branch for Breast Cancer) participating centres and the [1]Janssen Research Foundation, The Netherlands*

Liarozole is an aromatase inhibitor that inhibits the P450-dependent catabolism of retinoic acid.

Methods: A study of Liarozole was performed from Sep 94 to Apr 98 in 110 postmenopausal patients with MBC belonging to four prospectively defined groups; *1) TAM refractory* ER+, PFS < 1 yr (adj TAM) or <4 mo (TAM for MBC), no prior CT for MBC *2) CT resistant* any ER status, 1–2 prior CT regimens, ≤2 prior HT regimens *3) HT resistant* ER+/?, 1–2 prior HT regimens, PFS ≥ 1 yr for adj HT (ER+), ≥2 yr for adj HT (ER?), ≥4 mo for HT for MBC, no prior CT for MBC *4) ER negative* no prior CT or HT for MBC. Liarozole was administered orally at a dose of 150 mg bid. Dose escalation to 300 mg bid was abandoned in Aug 96.

Results: Toxicity was consistent with retinoid activity: skin, fatigue, nausea/vomiting, stomatitis, alopecia. 4% of patients had possibly related cardiac events. 24% of patients discontinued therapy due to toxicity.

Response	1 n = 16	2 n = 33	3 n = 36	4 n = 25	All patients n = 110
CR (%)	0	0	6	4	3
RR (%)	0	12	17	8	11
Clinical benefit (%)	0	15	25	16	16

Responses were observed in soft tissue, bone, lung and liver. Median duration of response was 11.5 mo (range 2.2–26.8).

Conclusions: Liarozole is an active compound in patients with MBC including those who are not traditional candidates for HT, but it is poorly tolerated by the majority of patients. New analogues of this compound should be investigated.

73 ORAL

Gamma linolenic acid with tamoxifen as primary therapy in breast cancer

F.S. Kenny[1], S. Pinder[2], I.O. Ellis[2], R.P. Bryce[3], J. Hartley[3], J.F.R. Robertson[1]. *[1]Departments of Surgery; [2]Pathology Nottingham City Hospital; [3]Scotia Pharmaceuticals Limited, Stirling, UK*

Purpose: Gamma linolenic acid (GLA) has been proposed as a valuable new cancer treatment having selective anti-tumour properties with negligible systemic toxicity. Proposed mechanisms of action include modulation of steroid receptor structure and function. This is the first study to investigate the effects of GLA combined with hormone therapy in an endocrine sensitive cancer.

Methods: 38 patients with elderly primary (n = 20), locally advanced (n = 14) or metastatic (n = 4) breast cancer consented to take 8 capsules