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

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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

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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

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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

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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