Conclusion: Our study supports the prognostic impact of immunohistochemical detected cathepsin D expression in the epithelial component of breast cancer.

83 POSTER

A phase II study of a potent and selective aromatase inhibitor, anastrozole (ZD-1033), in Japanese postmenopausal women with advanced/recurrent breast cancer

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Purpose: This trial was conducted using two dose levels of 'Arimidex' (anastrozole) (0.5 mg or 1 mg once-daily), the aim being to determine the dose of anastrozole (ZD 1033) to be used in randomised comparative trials involving Japanese women.

Methods: The trial design was randomised, open-label, parallel-group. Patients were required to be postmenopausal with advanced/recurrent breast cancer. The primary endpoints were objective response and tolerability, with secondary endpoints including oestradiol (E2) measurements, and cortisol and aldosterone assessments.

Results: 73 postmenopausal patients entered the trial, 36 patients in the 0.5 mg group and 34 patients in the 1 mg group were eligible. Response rates (CR/PR) were 27.8% in the 0.5 mg group and 38.2% in the 1 mg group (n.s). Plasma E2 was significantly reduced from baseline with both doses of anastrozole (82% suppression with 0.5 mg and 81% with 1 mg being the maxium seen over the 12 week assessment period). There was no evidence of an effect upon adrenal steroidogenesis. Both doses of anastrozole were well tolerated (no toxicity's >grade 2), with no significant differences between the groups.

Conclusion: Based on the objective response data and oestradiol measurements, and since increased toxicity was not observed with the higher dose, anastrozole 1 mg was selected for further study in randomised comparative studies.

'Arimidex' is a trademark, property of Zeneca Limited

84 POSTER

The increasing of effect after discontinuation of the treatment with Taxotere in patients with breast cancer

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Purpose: 39 patients with morphologically proven advanced breast cancer were treated with taxotere. Taxotere was administered in dose 100 mg/m^2 every 3 weeks. As a premedication we used medrol instead dexametason.

Methods: 33 pts have received previously chemotherapy: neoadjuvant – 5 pts (2 – FAC, 3 – CMF), adjuvant – 23 pts (16 – CMF, 7 pts with anthracyclines), chemotherapy for advanced breast cancer had 18 pts (17 pts with anthracyclines, 1 pt – CMF).

Results: The results of treatment were the following: overall response was 20/39 (51.3%), CR – 3/39 (7.7%), PR – 17/39 (43.6%), SD – 7/39 (17.9%), PD – 12/39 (30.8%). 35% of pts achieved response after 3 cycles, and 100% – after 6 cycles.

Median survival overall group is 19.7 mo. One year survival is 82% of pts. The increasing of effect, that we observed in 6 pts after the stop of the treatment during follow up: in all 6 pts – after 3 mo, in 2 pts – after 6 mo. 1 pt achieved CR 3 mo later after treatment break. The duration of response was: PR from 9 to 25 mo, CR – 5 mo.

Conclusion: Taxotere is appears to be one of the most effective cytostatic agent against advanced breast cancer, and the effect can be increase after stop treatment. We consider the mechanism of this effect should be explain.

85 POSTER

Intratumoral focused chemotherapy with cisplatin/epinephrine injectable gel for palliative treatment of metastatic breast cancer

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Purpose: In a phase III study we are evaluating the safety and efficacy of intratumoral chemotherapy with cisplatin/epinephrine injectable gel (CDDP/epi gel) for local treatment of solid tumors of various histologies. The delivery system provides high tumor drug concentrations for extended periods.

Methods: Two identical, open-label studies enrolled patients with solid tumors who had failed previous therapy. CDDP/epi injectable gel was administered intratumorally (2 mg CDDP/cm^3 tumor) weekly for 6 weeks, or until objective complete response of all target tumors. Patients were then followed for 4 weeks. Evaluations included palliation or prevention of tumor-related symptoms for the most troublesome tumor (MTT), tumor response for the MTT and responses of all treated tumors (tumor response: ≥50% tumor volume decrease sustained ≥28 days), and adverse events.

Results: 30 patients with metastatic breast cancer represented the largest group of cancers treated in the ongoing study with 94 evaluable tumors (1–7 tumors/patient) treated to date. Total patient cumulative dose of 1 to 215 mg CDDP (median 27.4 mg) was administered in 1–6 intratumoral injections of CDDP/epi gel. Preliminary results show 6 of 30 (20%) patients had response of the MTT, and 11 of 30 (37%) patients had response of one or more tumors. Overall, 19/94 (20%) of all treated tumors had objective tumor responses. Treatment goals reflected the desire to improve function or disease management (wound care, pain control, tumor invasion). Ten of 30 patients (33%) attained the physician-selected primary treatment goal. Treatment with CDDP/epi gel was generally well-tolerated. Common toxicities (e.g., vomiting and nausea) of intravenous cisplatin were less frequent and easily managed with CDDP/epi gel.

Conclusion: Local tumor control with CDDP/epi gel provides a new therapeutic tool for management of solid tumors as a single modality and holds promise for use in combination with standard therapies.

86 POSTER

EORTC-IDBBC (Investigational Drug Branch for Breast Cancer): Seven years of active European collaboration

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IDBBC is a subgroup of the EORTC-Breast Group. The goals and a summary of the trials run till 1995 have been published recently (EJC 33: 1173, 1997). The following table summarizes the ongoing studies. More data from these studies will be presented at the conference.

Drugs	No. of pts Expected/entered	Comments
Doxo vs Doxo + CPA + Taxol	260/165	In collaboration with EORTC-ECSG (phase III).
Caelyx	32/14	6 week schedule (phase I–II). Accrual at 70 mg/m^2 is ongoing.
Docetaxel + Amifostine	21/18	Feasible. Toxicity of Docetaxel is less than expected!
Liarozole	116/110	Antitumor activity was seen. Significant GI and skin toxicity observed.
Exemestane vs Tamoxifen	100/39	First-line therapy (phase II).
Epirubicin (bolus) + CPA (bolus) + 5 FU (CI)	25/0 (feasibility)	Locally advanced disease. Escalating doses of Epirubicin.
Gemcitabine + 5 FU (CI)	15/0 (feasibility)	2nd or 3rd line therapy.

In parallel, the role of the MUGA scan in monitoring cardiac function, the pharmacokinetics of Docetaxel (± Amifostine) and Caelyx and the effects of Exemestane on the lipid profile and coagulation tests are under investigation.

87 POSTER

Topical use of Miltex® in patients with breast cancer's cutaneous manifestations

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Purpose: In patients with breast cancer's cutaneous manifestations first-line treatment includs local mamagement (surgical and/or radiotherapeutical). Also hormonal therapy and chemotherapy may be useful under certain clinical conditions. If traditional therapy is ineffective or impossible new

drugs and treatment methods are necessary. In a prospective study the value of Miltex® was evaluated.

Materials and Methods: Miltex® is topical formulation of 6% solution of miltefosine produced by ASTA Medica. Miltex® was used in 11 patients with advanced breast cancer's cutaneous metastases by standard posology (2 drops per 10 cm^2 once a day for the first week of treatment and then 2 drops per 10 cm^2 twice a day for at list 8 weeks).

Results: 10 patients were evaluated for response to treatment and 1 patient was lost to follow up. The objective response (in all patients partial remission) was obtained in 6 patients (60%). The best results were obtained in patients with superficial skin lesions.

Local side effects which may be connected with topical use of Miltex® were noted in 80% of treated patients. Dry skin, scale formation and sensation of tension were the most frequently occurred and they were not severe. In such cases a fat-based cream was used additionally with some success. The general condition of patients was unchanged.

It is very important to note the positive psychological effect connected with topical treatment of skin lesions.

Unfortunately, we observed the progression of disease except skin manifestations in some treated patients and in this connection the additional treatment was performed.

Conclusion: Miltex® is well tolerated and effective drug for the topical treatment of skin metastases of breast cancer. In some cases it is necessary to connect the topical treatment with system chemotherapy and/or hormonotherapy.

88 POSTER

Antitumor effects of 22-oxa-calcitriol on MDA-MB-231 tumors in athymic mice

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Purpose: 22-oxa-calcitriol (OCT) inhibits the proliferation of several tumor cells through binding to vitamin D3 receptor. The purpose of this study was to evaluate the usefulness of OCT for the treatment of hormone-independent breast cancer.

Method: We investigated antitumor effects of OCT and combined effects of OCT with 5'-DFUR on MDA-MB-231 tumors in female athymic mice. Additionary we examined changes of the angiogenic factor vascular endothelial growth factor (VEGF) in tumors.

Results: Dose-dependent decreases in tumor size were observed when various concentrations of OCT were administered. OCT at the dose of 0.1 microgram/kg or more significantly suppressed the growth of tumors. The combined effect of OCT with 5'-DFUR didn't exceed the effect of OCT alone. The expressions of VEGF analized by enzyme-linked immunosorbent assay were significantly decreased in the OCT-treated group.

Conclusion: OCT suppresses the growth of ER-negative MDA-MB-231 tumors. Antiangiogenic effect may play some part of this event.

89 POSTER

Efficiency of using the intensive regimen of chemotherapy with high doses of 5-fluorouracil in treating patients having breast cancer

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Purpose: The results of combined treatment of patients with breast cancer (BC) using neoadjuvant chemotherapy (NACh) with high doses of 5-fluorouracil (5-FU) were evaluated.

Methods: The investigation included 24 patients with nodule forms of BC of II–III stages (1) and 12 patients with edematous-infiltrating forms of BC the treatment of whom began with conducting 1–2 courses of NACh according to the scheme 5-FU at a dose of 1000 mg/m2 on the 1-st-5-th days by method of continuous 120-hour infusion, cyclophosphamide at a dose of 600 mg/m2 intravenously on the 1-st and 8-th days and methotrexate at 40 mg/m2 intravenously on the 1-st and 8-th days with a following operative intervention in the volume of radical mastectomy, adjuvant chemotherapy according to the scheme CMF and radiotherapy by indications.

Results: In total 70 courses of chemotherapy using high doses of 5-FU were performed. It has been shown that the studied chemotherapy regimen does not cause any masked toxic responses and has a good tolerance in patients. A direct clinical efficiency made up 89.2% in the 1-st group and 73.4% in the second one. The evaluation of therapeutic pathomorphism degree revealed increasing a number of potentially "lethal" mitoses and decreasing the mitotic activity of tumor cells. The 3-year metastatic-free survival rates by the groups made up 89.1 ± 7.4% and 63.7% ± 5.6% and the total survival rate was 95.1 ± 4.9% and 71.6 ± 4.7%, respectively.

Conclusion: The results obtained testify to great efficiency of using high doses of 5-FU in combined treatment in patients having BC.

90 POSTER

Outcome in patients with advanced breast cancer treated with anastrozole following loss of reponse to tamoxifen and megestrol acetate

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Background: A significant number of patients who receive tamoxifen for advanced breast cancer will have disease progression. Effective new therapies with minimal side effects are needed to treat patients with advanced breast cancer.

Aim: To study patients with advanced breast cancer who had progressed or lost response to tamoxifen and or megestrol acetate and who were subsequently treated with Arimidex, a non-steroidal selective aromatase inhibitor.

Patients & Methods: Between October 1996 and September 1997 we prospectively studied 20 patients with advanced breast cancer assessed by clinical examination, tumour marker CA 15-3 and imaging. All patients had been treated previously with primary or adjuvant tamoxifen or megestrol acetate.. Those who lost response to either or both of the above were given anastrozole 1 mg/day. Follow-up was at six weekly intervals.

Results: The median age of the patients was 69 years (range 35–93). Median follow-up was six months. Sites of recurrence or metastasis were lymph nodes (6), surgical scar (4), skin (8), bone (3) and peritoneum (1) Previous treatment comprised segmental/total mastectomy with axillary clearance (10), primary or adjuvant tamoxifen (20),

Cytotoxic chemotherapy (1), radiotherapy (4), megestrol (4). Clinical response in the form of shrinkage or disappearance of tumour or nodal mass, healing of fungating tumour was seen in 12 patients. CA 15-3 decreased in 7 and returned to normal in one patient. Three patients died during the follow-up period.

Conclusion: Anastrozole has been shown to benefit a larger group of patients than expected from the literature but this may be due to selection of patients who had been previously controlled with endocrine chemotherapy. Clinical examination and where this is not feasible CA 15-3 tumour marker may be a reasonable outcome measurement to identify such a subgroup which is likely to benefit.

91 POSTER

Intratumoral therapy with VRCTC-310 for refractory skin metastatic breast cancer. Preliminary report

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A natural product VRCTC-310, is derived from purified snake venom fractions. It is composed by crotoxin and cardiotoxin. It has shown activity against human tumors either by intramuscular route or by intratumoral route. Four patients (pts) with relapsed and refractory skin metastatic breast cancer were treated from May 1996 to November 1997, with VRCTC-310, 0.33 mg/m^2 by intratumoral route every week. All pts had confirmed histologic diagnosis of disease. As prior treatment, all pts underwent a surgical procedure, radiation therapy, no less than three lines of chemotherapy and hormonotherapy. A big thoracic tumoral mass was the main site for therapy. All pts gave informed written consent before treatment. Peritumoral multiple disseminated nodular lesions served as control. The VRCTC-310 dose was diluted with 1 ml of lidocaine and it was injected into the skin tumoral mass in four different quadrant every 7 days. Objective response was registered in two pts (CR 1, PR 1). Local pain at the injection site, spontaneously reversible, was the only side effect. Most of nodular satellite lesions reduced in size or disappeared during treatment. Because of the lack of limiting toxicities, VRCTC-310 appears as an useful contribution for the treatment of refractory skin metastatic breast cancer. These results, make the regimen feasible for out-patient treatment and further studies using the above-mentioned approach are warranted.