

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<sup>2</sup> once a day for the first week of treatment and then 2 drops per 10 cm<sup>2</sup> 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

H. Matsumoto<sup>1</sup>, Y. Iino<sup>2</sup>, Y. Koibuchi<sup>1</sup>, M. Maemura<sup>1</sup>, J. Horiguchi<sup>1</sup>, H. Takei<sup>1</sup>, H. Nagaoka<sup>1</sup>, J. Ninomiya<sup>1</sup>, T. Yokoe<sup>2</sup>, Y. Morishita<sup>1</sup>. <sup>1</sup>Second Department of Surgery; <sup>2</sup>Department of Emergency and Critical care Medicine, Gunma University School of Medicine, Maebashi, Japan

**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. Additionally 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 analyzed 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

E.M. Slonimskaya, S.V. Kolesnikov, V.V. Kanasyova, E.Yu. Garbukov, R.A. Shagiakhmetova. Department of General Oncology, Cancer Research Institute of Tonsk, Russia

**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/m<sup>2</sup> on the 1-st-5-th days by method of continuous 120-hour infusion, cyclophosphamide at a dose of 600 mg/m<sup>2</sup> intravenously on the 1-st and 8-th days and methotrexate at 40 mg/m<sup>2</sup> 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 response to tamoxifen and megestrol acetate

F. Mihaimeed, S.M. Kelleher, S. Parbhoo. Breast Unit & Cancerkin, University Department of Surgery, Royal Free Hospital & School of Medicine, London NW3 2QG, UK

**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

L. Costa<sup>1</sup>, H. Miles<sup>2</sup>, C. Araujo<sup>2</sup>, V. Villarrubia<sup>3</sup>. <sup>1</sup>Ventech Res.; <sup>2</sup>Hosp. B. Houssay, Bs. Aires, Argentina; <sup>3</sup>Cantabria Inc., Madrid, Spain

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<sup>2</sup> 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.