vitro growth kinetics. On the other hand, MX-1 cells were growing much slower than the above cell lines.

Discussion: Our study shows that human breast cancer cell lines exhibit a different expression pattern of the urokinase plasminogen activator system components but a link between this expression and their *in vitro* growth capacity could not be demonstrated. Our findings of higher PAI-1 amount in combination with a higher growth rate by BT-20 cells are in line with the proposed protective mechanism against the proteolytic degradation of tumor cells themselves mediated by PAI-1. Based on our observation that non-PAI-1 producers, MCF-7 cells, also exhibited a high growth capacity we suggest, that disturbance of balance between activator and inhibitor may also result in upregulated *in vitro* tumor growth. Therefore, a direct role of PAI-1 in growth rate of breast carcinoma is, at least *in vitro,* rather unprobable.

P14 Adjuvant tamoxifen treatment in breast cancer induces no activation of blood coagulation

C. Oberhoff, U.H. Winkler, A.E. Schindler. *University Hospital Essen, Dept. of Gynecology, D-45122 Essen, Germany*

Based on the incidence of thromboembolic complications (1–14%) during the clinical adjuvant breast cancer trials, tamoxifen is considered as a potentially thrombogenic drug. Studies evaluating changes of hemostasis during tamoxifen treatment report very conflicting results and the cause-and-effect relationship has never been established.

To asses potential effects of antiestrogen treatment on the hemostatic system, we studied blood coagulation and fibrinolysis in 20 postmenopausal women with breast cancer receiving 20 mg tamoxifen daily as an adjuvant therapy. Blood sampling was done before and after the 1st, 3rd and 6th month of treatment. Blood collection was done according to standard protocols.

Pretreatment values of procoagulation [fibrinogen (Fbg), factor VII (FVII)], thrombin-antithrombin-complex (TAT), anticoagulation [antithrombin III (ATIII), protein C (PC), protein S (PS)] or plasminogen and plasminogen activator inhibitor were found within the normal range, whereas tissue-plasminogen activator (t-PA), D-dimer fibrin degradation products (DDIMER) and prothrombin-fragment 1 + 2 (Frag 1 + 2) were elevated. On therapy an initial decrease of all measured parameters was observed during the first month of treatment, followed by consistent plasma levels up to the end of the observation period. This effect was significant for Fbg, FVII, AT III, PC, PS and t-PA. Fibrin degradation products decrease continuously. The analysis of blood coagulation inhibitors revealed decreased AT III (13%), PS (27%) and PC (29%) during the first month of treatment. However, all values remained within the normal range (>70%). No cumulative effects on anticoagulation were seen on therapy.

Our pretreatment data are consistent with an activated hemostatic system (acute-phase-reaction) after major surgery. We can not exclude, that the decrease of hemostatic parameters during the initial phase of tamoxifen treatment refers to the timing of blood collection (<14 days after surgery). The decrease of blood coagulation inhibitors was not associated with a concomittant increase of in vivo coagulation markers (Frag 1 + 2, TAT, DDIMER). Therefore our results are likely to reflect only the resolution of postoperative activation and does not translate into a drug related thrombogenic effect. The epidemiological findings suggesting an increased risk for thromboembolic complications may easily be explained by tumor-induced hypercoagulability, additional anti-tumor therapy or individual predisposing risk factors for thrombosis (inherited or defects of blood coagulation).

P15 Blood coagulation and fibrinolysis after oral or intravenous cyclophosphamide containing adjuvant CMF-chemotherapy

C. Oberhoff, U.H. Winkler, A.E. Schindler. *University Hospital Essen, Dept. of Gynecology, D-45122 Essen, Germany*

Epidemiological data suggest an increased incidence of thromboembolic complications (2–17%) during CMF-chemotherapy in breast cancer patients. Several studies report a decrease of blood coagulation inhibitors (protein C and S) induced by adjuvant CMF-chemotherapy containing oral application of cyclophosphamide. Because of an increased alkylating activity after oral administration, the aim of our study was to asses potential different effects of oral (p.o.) and intravenous (i.v.) application of cyclophosphamide during adjuvant CMF-Chemotherapy for breast cancer.

We studied parameters of blood coagulation and fibrinolysis in 20 patients receiving 6 courses of chemotherapy containing of cyclophosphamide (100 mg/m^2 p.o. days 1–14 or 600 mg/m^2 i.v. days 1, 8), methotrexate (40 mg/m^2 days 1, 8) and 5-fluorouracil (600 mg/m^2, days 1, 8). Blood collection was done before the application of the chemotherapy at days 1 and 8 according to standard protocols.

In both treatment groups the pretreatment values of procoagulation [fibrinogen, factor VII (FVII)], anticoagulation (antithrombin III, protein C (PC), protein S (PS), fibrinolysis (plasminogen, tissue-plasminogen activator) and antifibrinolysis (plasminogen-activator-inhibitor) were found within the normal range. Thrombin-antithrombin-complex and D-dimer fibrin split products were elevated. On therapy a decrease of FVII (20–35%), PC activity (20–40%) and antigen (25–38%) was observed from day 1 to 8 in both treatment groups. This effect was only significant ($p < 0.005$) for protein C. Whereas the plasma levels of FVII returned to pretreatment values within the treatment free period, a distinct cumulative effect was demonstrated for protein C with the occurrence of pathological values below 60% of normal range. There was no significant difference within the two treatment groups, but the effect was pronounced with oral cyclophosphamide.

Our data confirm the results of other authors reporting an acquired deficiency of protein C associated with adjuvant CMF-chemotherapy. We observed no significant difference whether cyclophosphamide was given p.o. or i.v.. In absence of any significant cumulative decrease of other vitamin-K-dependent coagulation factors (FVII, PS), the simultaneous decrease of PC activity and antigen, indicates a specific defect of the vitamin-K-dependent synthesis of protein C in the liver. Further analysis is mandatory to evaluate if cyclophosphamide, methotreaxate or 5-fluorouracil cause this effect.

P16 Adjuvant Goserelin depot in premenopausal women with early breast cancer: Ovarian function, bone mineral density and survival. Preliminary data

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

Ovary suppression with Goserelin depot is alternative to ovarian ablation: in metastatic breast cancer Goserelin depot yelded objective response in 36% of patients. Ovarian ablation in women aged under 50 was associated with 6% fewer recurrences or deaths after 15 years. Studies are ongoing in order to evaluate the effectiveness of Goserelin depot as adjuvant treatment in the prevention of relapse and reduction in mortality.

We report our experience about 75 premenopausal patients with early breast cancer treated after surgery with Goserelin depot 3.6 mg subcutaneously every 28 days for two years. Median age was 43 years (range 31–50), all patients had regular menses, 36 patients were N+ and 39 were N−. ER status was positive in all patients but one in which was unknown.

One patient had bilateral breast cancer.

Owing to administration of Goserelin depot amenorrhea occurred after the first depot in 11 patients and after the 2nd depot in 64 women.

Spotting was observed in 8 patients and stopped after 10 depots.

At the end of 26 depots regular menses resumed in most patients (73%), on average after 5.3 months.

Weight gain was observed in 61% of patients, in 28.1% of patients weight was unchanged, weight loss occurred in the remaining women. All patients complained of hot flushes, sweating and impairment of libido. Metrorrhagia occurred in 3 patients at the end of therapy: 2 patients underwent hysterectomy. A decline in Bone Mineral Density was observed in patients studied with Dual Energy X-ray Absorptiometry (DEXA). A second primary tumor occurred in four patients: myeloid chronic leukemia, kidney cancer, oat cell carcinoma, second primary breast cancer. At a median follow-up of 51 months overall survival was 90.5% and disease free survival 70.2%.

P17 Weight gain associated with breast cancer adjuvant chemotherapy

G. Fried, K. Drumea, N. Yereslav, B. Vizel, N. Haim. *Department of Oncology, Rambam Medical Center, Haifa, Israel*

Purpose: Weight gain (WG) is one of the most common, distressful and less appreciated toxicity of adjuvant chemotherapy (CT) of breast cancer (BC). We retrospectively evaluated WG in the adjuvant CT of BC associated with cyclophosphamide, methotrexate, 5-fluorouracil (CMF) or cyclophosphamide, doxorubicin, 5-fluorouracil (CAF).

Methods: The pretreatment and post-treatment weight was determined in all patients and was recorded in the file.

Results: Between 1/94 and 12/95 131 BC pts were treated at our center with adjuvant CMF or CAF. Data were available for 65 CMF and 24 CAF treated pts. WG (range: 1–20, median, 8 kg) was recorded in 62 pts (70%). Weight loss (range: 2–9, median, 4 kg) was recorded in 10 pts (11%) and the remaining 17 pts (19%) maintained their weight during CT. WG was more pronounced in CMF than in CAF (51 pts, 78% vs 11 pts, 46%, $p < 0.004$). WG of >10 kg was noticed in 22 CMF treated pts (34%) vs 2 CAF treated pts (8%). Other factors that significantly affected WG included menopausal status {80% in pre vs 43% in postmenopausal ($p < 0.004$)} and obesity before therapy {100% for pts with pretreatment weight >130% of ideal body weight (IBW) vs 36% for pts with weight <130% IBW ($p < 0.0002$)}. There was no significant influence on WG for the type of surgery (lumpectomy vs mastectomy) or for CT induced amenorrhea.

Conclusion: WG is a common side effect of adjuvant CT for BC and its