P79 Three new highly active cisplatin-containing combinations in locally-advanced (stage III) and locally-recurrent breast carcinoma. A phase II randomized study

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We designed three new four-drug cisplatin-containing combinations to be tested in breast carcinoma. All schedules included methotrexate (M) on day 1 and cisplatin (P) on day 2, as in the classical MVAC combination, and differed from one to another in the addition of other two drugs among epirubicin (Epi), vincristine (V), etoposide (E), mitomycin (Mi). This study was a further development of the cisplatin/etoposide combination, which was shown to be very active in metastatic (Cocconi et al.; JCO 1991; 9: 664) and of the classical MVAC combination, which was confirmed as very active even in breast carcinoma (Bisagni et al.; Annals of Oncol. 1994; 5: 93). We randomly administered these combinations, named MPEpiV, MPEpiE, MPEMi, to 101 patients with stage III (57) or with locally-recurrent breast carcinoma (44). After 4 cycles, patients received local treatment, surgery and/or radiotherapy. The toxicity of the three combinations was substantial but treatment was tolerable and no toxic deaths were observed. Bone marrow suppression, vomiting and mucositis were the most important side effects. The short-term objective response was very high, with no significant differences among the three schedules. Including in the denominator all 101 patients in an intention to treat analysis, the overall CR rate was 23%, and the CR plus PR rate 86%. In stage III, at time of surgery, 7 of 57 patients showed pathological CR (12%). Even the long-term results appeared as favourable compared with those usually reported in the literature in these situations. After a median follow-up of 56 months, in stage III disease 3 yrs and 5 yrs RFS were 60–49% and 79–63% respectively; in locally recurrent disease RFS were 40–26% and 89–64%.

In conclusion, these three new so-called MVAC-like combinations appeared very active in treating stage III and locally-recurrent breast carcinoma. Our results warrant further investigations using these schedules, compared to conventional chemotherapies, in phase III studies concerning metastatic disease and adjuvant/neoadjuvant setting.

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P80 Neoadjuvant chemotherapy in locally-advanced breast cancer: A preliminary report

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Eighty-five patients with locally-advanced (stage III) breast cancer were recruited to the study. Thirteen patients were subsequently excluded during follow-up. The median age was 50 (range: 28–70) in the remaining 72 patients. There were 33 premenapausal and 39 post-menapausal patients. The treatment protocol consisted of 3 consecutive cycles of neoadjuvant CEF (cyclophosphamide 500 mg/m2/d on day 1, epirubucin 50 rng/m2/d on day 1 and fluorouracil 600 mg/m2/d on day 1, to be repeated every 3rd week). Response to treatment was evaluated as a reduction of the initial size of breast mass evaluated by physical examination and mammography. In case of CR and PR, 4th cycle of CEF was given followed by modified radical mastectomy, 5th CEF, radiotherapy and 3 cycles of CMF chemotherapy, respectively. We obtained 16 (18.8%) CR, 60 (70.6%) PR, 7 (8.2%) stable disease and 2 (2.4%) progressive disease. Median disease-free survival (DFS) durations were 19.58 and 21.54 months in premenapausal and post-menapausal patients, respectively. Median overall survival (OS) durations were 19.64 and 22.78 months in these patients. In overall patient group, median DFS and OS durations were 19.78 and 21.54 months, respectively.

Further follow-up is needed to evaluate the results of this treatment protocol.

P81 Using high doses of 5-fluorouracil in patients with breast cancer: 3-Year results of the treatment

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The aim is studying the effectiveness of using the intensive regime of chemotherapy with high doses of 5-fluorouracil in treating patients having breast cancer (BC).

Material and Methods: There have been treated 24 patients with nodular forms of BC II (12) and III (12) stages of a disease. The treatment included the conducting of preoperative chemotherapy according to the scheme: 5-fluorouracil at a dose of 1000 mg/m2 per day as 120-hour infusion i/v on the 1-st to the 5-th days; methotrexate at a dose of 40 mg/m2 and cyclophosphamide at a dose of 600 mg/m2 on the 1-st, 8-th days. After performing a radical mastectomy in the postoperative period 5–6 courses of chemotherapy using the scheme CMF and radiotherapy by indications were also carried out. The control group consisted of 66 patients with BC having got a standard chemotherapy course according to CMF scheme in the preoperative regime.

Results: The efficiency of the neoadjuvant chemotherapy made up 79.2%, treatment without any effect was marded in 20.8% of patients. In the control group these indices corresponded to 53% and 47%. The most expressed effect of treating was observed in women younger than 50 years with a normal menstrual function. The results of the treatment did not depend on the histological type of a tumor. For patients having got the intensive regime of treatment the 3-years survival rate without signs of the tumor recurrence made up 95%, without metastases it was 90%. In the control group these indices made up 86.2% and 69.8%, respectively.

Conclusion: The obtained results testify to a high effectiveness of the proposed regime of neoadjuvant chemotherapy.

Friday, February 27, 1998 9.00–18.00

Adjuvant Conventional Chemotherapy

P82 Comparison of doxorubicin/cyclophosphamide versus doxorubicin/cyclophosphamide/tamoxifen and CMF-chemotherapy versus tamoxifen in node positve breast cancer. An up-date of the German adjuvant breast cancer group (GABG) trial

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Goal: To assess the effectivity of chemotherpy (CT) versus CT + Tamoxifen in a high risk (HR) group and CT versus Tamoxifen in a low risk (LR) group of women with node positive breast cancer.

Patients and Methods: Based on the extent of axillary lymph node involvement and hormone receptor status, patients were recruited to the LR and HR arm of a trial run between 1981 and 1986. Patients with oestrogen and/or progesterone receptor (R) positive ($\geq$20 fmol) tumors with less than 4 involved lymph nodes (n = 276) were randomized to either tamoxifen 3 × 10 mg/day for 2 years or 6 cycles of cyclophosphamide 500 mg/m^2, methotrexate 40 mg/m^2 and 5-fluorouracil 600 mg/m^2, all day 1 + 8 (CMF) intravenoulsy (i.v.). Patients with R negative tumors or more than 3 nodes involved were randomized to 8 cycles of doxorubicin 30 mg/m^2 day 1 plus cyclophosphamide 300 mg/m^2 day 1 + 8, (AC) i.v. or 8 times AC plus tamoxifen 3 × 10 mg/die orally for 2 years.

Results: In this up-dated analysis of a follow up of 10 years no difference in clinical outcome could be observed in the LR group. However in patients <50 years of age CMF significantly improves disease-free (DFS)(p = 0.05, log rank test) and overall survival (OS)(p = 0.008), whereas patients >50 years tamoxifen was more effective (DFS: p = 0.001, OS: p = 0.05). Due to this retrospective stratification and an imbalance of the age distribution in the 2 treatment arms these results have to be interpreted with caution. In the HR group a significantly prolonged disease-free survival (p = 0.03) and a trend for a longer overall survival (p = 0.1) for patients >50 years with the chemoendocine treatment. The same was found for patients with positive R (DFS:p = 0.03 and OS: p = 0.5).

Conclusions: The effect of chemo- and endocrine therapy in node positive breast cancer is dependent on patients age and the receptor content of the primary. CT is effective in younger patients, the combination represents the best choice for patients >50 years of age.

P83 Dose effect of epirubicin in amenorrhea induced by chemotherapy for breast cancer

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Purpose: To demonstrate the role of Epirubicin combined with Cyclophosphamide and 5 Fluorouracil (FEC regimen) in amenorrhea induced by chemotherapy.

Population: 269 premenopausal patients received FEC in neoadjuvant and/or adjuvant setting for breast cancer. Epirubicin was utilized at 50 mg/m^2, 75 mg/m^2 or 90 mg/m^2.

Method: amenorrhea was defined as discontinuation of menses for at least 60 days from the first day of the last menses. Mean dose (mg/m^2) of Epirubicin and Cyclophosphamide received at onset of amenorrhea, total dose of these two drugs administered were recorded. Dose intensity (dose/time) was evaluated