P69 The effect of preoperative irradiation therapy and adjuvant chemotherapy for clinical stage III breast cancer

A. Mudėnas, V. Špikalovas, S. Bružas, A. Lukšytė, J. Kurtinaitis. *Lithuanian Oncology Center, Vilnius, Lithuania*

Introduction: the aim of this study was performed to examine the efficacy of combined: radio and chemotherapy in patients with extensive axillary disease (N) and large primary tumor (T).

Patients and Methods: a total of 53 patients with operable breast cancer of stage p $T_3N_+M_0$ were entered in this trial between 1987 and 1994. For all patients was given preoperative irradiation of axilla, supra-infraclavicular region with a daily dose of 20 Gy, 5x/week to a total dose of 40–45 Gy and underwent radical or modified mastectomy 2 or 3 weeks after the completion of radiotherapy. All patients received irradiation of parasternal LN with 40–45 iGy by interstitial neutron radiotherapy.

A total of 53 patients received 6 cycles of adjuvant systemic CMF (Cyclophosphamide 100 mg/m^2 days 1–14, Methotrexate 40 mg/m^2 days 1 and 8,5-Fluorouracil 500 mg/m^2 days 1 and 8 within 30 days of primary surgery).

Results: Analysis of survival (S) showed, that 5 years survival for the stage III was 65%. According to axillar LN status N_2 – 5 years survival was 56%.

Conclusion: preoperative radiotherapy significantly reduces the incidence of local–regional recurrence and postoperative adjuvant chemotherapy has improved the disease free survival and survival.

Friday, February 27, 1998 9.00–18.00

Primary Chemotherapy

P70 5-Year results of combined modality approach in locally advanced breast cancer (LABC). Analysis of prognostic factors

M. Zambetti, P. Quattrone, P. Verderio, S. Oriana, P. Valagussa, M. Terenziani, R. Zucali, G. Bonadonna. *Istituto Nazionale Tumori, Via Venezian 1, 20133 Milano, Italy*

Combined modality therapy with preoperative chemotherapy (PC: adriamycin, 75 mg/m^2 or epirubicin, 120 mg/m^2 q. 3 wks) followed by surgery (conservative, 28 pts; radical, 56 pts) and adjuvant CMF for 6 cycles (cyclophosphamide, 600 mg/m^2; methotrexate, 40 mg/m^2; fluorouracil, 600 mg/m^2 on day 1 and 8, q. 4 wks) was administered in 88 women with LABC (T_{3b}–T_{4a-c}) treated at the Istituto Nazionale Tumori, Milano, from February '91 to July '94. Treatment was completed with postoperative radiotherapy on residual breast or chest wall and tamoxifen was also given to 38 patients. Half of patients presented with unfavorable clinical signs (erithema or edema >1/3 of the breast and/or N_2 status). After PC, objective remission was achieved in 70% of cases, including 3 pts with clinical complete response. At a median follow up of 52 mos, the 5-year relapse-free survival (RFS) is 52.5%. None of the factors analyzed at diagnosis (T size, clinical nodal status, clinical presentation, menopause, ER, PgR, grading, Mib1) was able to predict response to PC. In univariate analysis extent of nodal status, residual tumor size, receptor status and Mib1 values, as assessed on surgical specimens, significantly influenced the 5-year RFS. Cox regression analysis revealed that the extent of nodal involvement remained the most important prognostic factor (HR 5.3), followed by Mib1 value (HR 4.5) and estrogen receptor status (HR 2.4). Present results indicate that: 1) single agent full-dose anthracycline treatment can achieve a response rate comparable to a conventional combination regimen; 2) in our case series no factor, clinical or biologic, determined at diagnosis is able to predict the resistance to PC with anthracyclines; 3) RFS is influenced by known prognostic factors. In this subgroup of patients, newer and more effective combination regimens are needed in order to achieve a high rate of clinical and pathological complete remissions which are an important marker of final treatment outcome (Bonadonna G. et al, JCO, 1998).

P71 Epirubicin (EPI) and vinorelbine (VNR): A new promising combination for primary systemic chemotherapy for breast cancer

C. Nisticò, A. de Matteis, R. Valenza, D. Quattrocchio, C. Garufi, A. Maiorino, M. Cremonesi, E. Rossi, B. Agostara, B. Lazzaro, A.M. Biorzacchini, A.M. D'Ottavio, R. Mencacci, E. Terzoli. *NAVE GROUP; Istituto Regina Elena, Viale Regina Elena, 291 Roma, Italy*

Neoadjuvant/adjuvant chemotherapy studies generally employ regimens that have appeared to be the most active against the same tumor in advanced stages. In a previous study, we showed the efficacy and tolerance of EPI and VNR plus G-CSF in untreated metastatic breast cancer patients, obtaining a 77% response rate (ASCO '97). We therefore wanted to examine this combination in a neoadjuvant setting. Beetween January 1997 and September 1997, 33 patients (pts.) with locally advanced breast cancer were treated with EPI, 60 mg/m^2 on days 1 and 15 and VNR 25 mg/m^2/week plus G-CSF; 150 mcg/m^2 on days 2, 4, 9 and 11. Six cycles of this therapy were administrated.

Patient Data: Median age: 51 years (range: 33–72 yrs.), PS:; 33 pts.; Premenopausal status: 17; Postmenopausal status: 16. The diagnosis of a carcinoma was always confirmed by cytology.

Toxicity: All the pts. are evaluable for toxicity. Neither febrile neutropenia nor infection were observed, although grade 3–4 neutropenia affected 12 pts. (36%). No other serious hematologic toxicity was present. With the exception of one pt. with grade 3 gastrointestinal toxicity, no other grade 3–4 toxicity was encountered.

Results: response was evaluated in 25 pts. A patholcgical complete response (CR) was opteined in 3 pts. (12%), a partial response (PR) in 21 pts. (84%) and stable disease (SD) in one pts. (4%). The overall response rate was 96%. There were no cases of progressive disease (PD). The clinical, radiological and pathologic evaluations were concordant in 14 of the 25 pts. (56%) and discordant in 11 (44%). Conservative surgery could be performed in 6 of the pts. (24%).

Conclusions: The combination of EPI; VNR and G-CSF appears to be highly effective and well tolerated in a neoadjuvant setting.

P72 Meta-analysis of dose intensity in breast cancer neoadjuvant chemotherapy (1985–1997)

Y. Shparyk. *Lviv Cancer Center, P.O. Box 2468, Lviv, 290029, Ukraine*

Dose intensity (DI) in chemotherapy is defined as the amount of drug delivered per unit time and is usually standardized to body surface area as mg/m^2/wk. A positive relation between DI and treatment outcome has been demonstrated not only in advanced breast cancer (BC) but also in adjuvant setting (Hryniuk). Only few trials using DI concepts have been performed in neoadjuvant chemotherapy for BC. To determine if chemotherapy DI influences treatment outcome in BC, 44 published trials (8 randomized trials included two arms) from 1984–1997 (including ASCO-97) were retrospectively analyzed (4857 patients). Regimens included such agents as Cyclophosphamide (43 trials) or Tiotepa (1), Fluorouracil (34), Doxorubicin (28) or Epidoxorubicin (20), Methotrexate (13), and Vinca alkaloids (9, Vincristine-7) (from single drug therapy to five-drugs combinations). Relative DI (RDI) of each study regimen was calculated against commonly used doses of each drugs in single regimens (e.g 25 mg/m^2/wk for Doxorubicin, 400 mg/m^2/wk for Cyclophosphamide, 25 mg/m^2/wk for Methotrexate, etc.). Meta-analysis of chemotherapy trials for BC with some various regimens have suggested that higher total RDI correlated strongly with improved response rate (51 trials, $r = 0.43$, $p = 0.0016$) and complete response (40 trials, $r = 0.42$, $p = 0.0065$). A randomized controlled trial targeted for DI itself will be necessary to confirm the usefulness of DI concepts in neoadjuvant chemotherapy in BC.

P73 Neoadjuvant therapy in stage II with T≥4CM and stage III breast cancer

K. Enomoto, T. Ikeda, A. Matsui, M. Kitajima, J. Koh, S. Masamura, T. Kinoshita, H. Ishikawa. *Dept. of Surgery Keio University, Tokyo, Japan*

The object of this trial was to compare neoadjuvant therapy with conventional postoperative adjuvant therapy in stage II with tumor size ≥4 cm and stage III breast cancer.

This randomiged trial has been conducted in collaboration of 15 Keio University affiliated hospital in Japan, during 33 months from April 1995 to December 1997. Both treatment arms consisted of five courses of EC (Epirubicin 50 mg/m^2 + Cyclophosamide 200 mg/m^2) courses were every 21 days for a total of five courses and daily administration of 400 mg of UFT and 20 mg of tamoxifen were continued for two years.

One of the arms consisted of two courses of EC were admistered before surgery and 3 courses after surgery. Another arm (B-arm) consisted of five courses were admistered after surgery.

So far, 50 patients were enrolled in this trial and they were allocated into either A or B method with minimization method based on age, stage, and estrogen receptor positivity, Key will be opened and interim analysis will proceeded in January 1998. Results from those analyses will be reported at this meeting in February 1998.