PP-5-3 High Dose Chemotherapy (HDCT) with Autologous Blood Cell (BC) Support in Metastatic Breast Cancer (MBC)

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Phase II study using HDCT with BC support was conducted to evaluate the toxicity and efficacy in patients suffering from MBC. 70 mg/m^2 Mitoxantrone, with 6 g/m^2 Cyclophosphamide and 12 mg/m^2 Vinblastine or 800 mg/m^2 Carboplatin followed by BC transplantation was used. The BC were obtained after induction chemotherapy consisting of FAC or FEC and subcutaneous administration of 5 μg/kg BW GM-CSF or 10 μg/kg BW G-CSF with standard apheresis. Over 80 chemosensitive patients were treated, median age 38 years. The median time from reinfusion to recovery of ANC to $\geq$ 0.5 nL was 11.5 days; to unmaintained platelet count of > 20/nL 12 days. No toxic deaths occurred. Sixty-nine patients are evaluable for response (23 CR; 46 PR) and are evaluable for long term survival at the median observation time of 24 months. The median survival is 33 months, the probability of survival at 54 months is 44%. The data so far indicate that this treatment strategy is safe and active in patients with MBC, can be delivered in an outpatient setting and show an advantage compared to historical controls. Only a prospective randomized study can establish the role of this treatment modality.

PP-5-4 Does Tamoxifen (Tam) Increase Bone Resorption in Premenopausal Women?

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Oestrogen is necessary for the maintenance of bone mass in premenopausal women. The antioestrogen Tam may potentially antagonize bone formation in premenopausal women leading to increased bone breakdown. To determine the effect of Tam on bone resorption, 40 females entered into the prevention trial have provided urine at baseline prior to entry and at 6 months on treatment. Urinary free deoxypyridinoline and Ctelopeptide of type I collagen (crosslaps), sensitive markers of bone resorption, have been measured using commercial kit assays. In 19 postmenopausal females Tam decreased urinary crosslaps compared to placebo. In 21 premenopausal women at 6 months, urinary crosslaps fell significantly from baseline in Tam and placebo but did not differ between groups.

Tam acts as an oestrogen on postmenopausal bone and does not antagonise oestrogen in premenopausal bone. Its use in premenopausal females will not lead to increased osteoporosis.

PP-5-5 CMF vs Tamoxifen (TAM) Plus Goserelin (GOS) as Adjuvant Treatment of ER Positive (+VE) Pre-Perimenopausal Breast Cancer Patients (PTS). Preliminary Results of an Ongoing Italian Breast Cancer Adjuvant Study Group (GROCTA) Trial

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A prospective trial was initiated in 1989 limiting trial entry to pre-, perimenopausal pts with node +ve ER +ve tumors. 235 pts have been entered so far and randomly allocated to receive either 6 cycles of standard CMF (CYC: 100 mg/sqm os dd. 1–14; MTX: 40 mg/sqm dd. 1, 8; 5-FU: 600 mg/sqm dd. 1, 8: every 4 wks) or 5 years of TAM at a daily dose of 30 mg plus GOS for the first two years. Main characteristics of study pts: CMF arm (no. = 113): median age, 45 (32–58); premenopausal, 89%; pT1, 49%; G1-2, 62%; node +ve $\geq$ 4.23%; QUART, 43%; TAM + GOS arm (no. = 118): median age, 46 (30–57); premenopausal, 88%; pT1, 40%; G1-2, 64%; node +ve $\geq$ 4.28%; QUART, 38%. At a median follow-up time of 36 months (0.5–70) 52 pts have relapsed (29, CMF; 23, TAM + GOS: n.s.) and 18 pts have died (9 pts in each group). 5-yr DFS was 56% in the CMF arm and 62% in the TAM + GOS arm (n.s.). 5-yr overall survival was 80% and 78% respectively (n.s.). Relapse rates were comparable in all nodal subgroups. Sixty-seven out of 95 evaluable pts in the CMF arm developed drug-induced amenorrhea. No difference was evident at 4 yrs between the DFS of pts in the TAM + GOS group and in the CMF group when only pts developing drug-induced amenorrhea were considered (CMF, 68%; TAM + GOS, 72%). However, 4-yr DFS of pts still menstruating in the CMF group was 52% (p = 0.07). *Conclusions:* 1) TAM + GOS was safe and equally effective as CMF with significantly less acute side effects; 2) although an adequate CMF dose intensity (DI) was employed in our study (median actual DI/planned DI: CYC: 84%; 5-FU: 87%; MTX: 88%), drug-induced amenorrhea was responsible at least in part of CT efficacy; 3) the use of ovarian ablation in combination with CT might be of benefit in those pts who don't achieve drug-induced amenorrhea in course of CT.

PP-5-6 Castration and Tamoxifen Versus Chemotherapy (FAC) for Premenopausal, Node and Receptors Positive Breast Cancer Patients: A Randomized Trial with a 7 Years Median Follow Up

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Between 10/1983 and 10/1989, 162 premenopausal women were randomized to receive either 6 cycles of FAC (CT) every three weeks or hormonotherapy (HT): surgical or radiotherapic castration and Tamoxifen 30 mg for 2 years. All patients had an invasive, non pretreated, node positive, both receptors positive breast cancer. Exclusion criteria were metastatic disease, more than one year amenorrhea, cardiac dysfunction. Local radiotherapy was restricted to the breast in the FAC arm: after 3 sus clavicular relapses, regional irradiation was mandatory for all patients. Due to low accrual, the trial must be stopped in 1989. At that time, 153 patients were fully evaluable Prognostic factors were slightly unbalanced in the CT arm: SBR grade 3 (19 vs 9 in the HT arm) and more than 10 nodes (10 vs 4 in the HT arm). Median age was 45 years (29–57), 137 were premenopausal, 16 with recent amenorrhea. 69 patients received HT and 84 CT. Castration was obtained by surgery, radiotherapy or none in 53, 32 and 15% of cases respectively. Median duration of Tam was 26 months (9–70). CT was not completed for 5 patients, febrile neutropenia occurred in 11% of cycles, only one grade 2 reversible cardiac event was noted. 65% of women experienced amenorrhea. Relative dose-intensity was 87%. With a median follow up of 84 months, we observed 36 vs 12 relapses and 22 vs 10 deaths in the CT and HT arms respectively. Locoregional and distant metastasis but no controlateral breast cancer were more frequent in the CT arm. Disease free survival was significantly better at 7 years in the HT arm 82.8% (71–90) vs 55% (43–56), but this difference disappeared after adjustment to the number of nodes which was the most important factor in multivariate analysis. Overall survival was not different despite a trend for the HT arm 84% (74–91) vs 74% (63–82). These results underlined the absolute necessity to reevaluate the place of hormonal treatment in subgroups of premenopausal patients.

POSTER PRESENTATIONS

PP-5-7 Interest of Irradiation and AVCF Chemotherapy in 241 Node-Positive Stage II Breast Cancers: Late Results

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From 1975 to 1986, 241 N+ stage II breast cancers underwent surgery (180 modified radical mastectomies, 61 lumpectomies), then irradiation of breast, supraclavicular nodes and internal mammary chain (IMC) with tangent fields, electrons 10 MeV, Cobalt 60 alone or both (50 Gy) pre or post AVCF chemotherapy (6 or 12 cycles) consisting of 4-week cycles of doxorubicin 30 D1, vincristin 1 D2, fluorouracil 400 and cyclophosphamide 300 D3 to D6 (all mg/m^2). In 1994, the median follow-up was 130 months: The 15-year OS and DFS actuarial rates were 49 and 54%; 104 patients relapsed (7 local, 11 controlateral, 86 metastatic). A multicentric randomized French trial compared the same AVCF with a more classical CMF (Misset, accepted in JCO) and showed comparable results at 15 years with a significant advantage for AVCF in OS (56 vs 41%) and DFS (53 vs 36%). 5 early cardiac events occurred: 1 tachycardia, 1 myocardial infarction and 3 congestive heart failures (CHF), of which 2 were fatal. In 1994, 62 patients accepted a late cardiac evaluation (clinical, ECG, echography). 4 events probably or certainly imputable to treatment were found: 2 left ventricular hypertrophies, 1 CHF, 1 chronic pericarditis. The cost/benefit ratio appeared satisfactory with an acceptable cardiac toxicity (not linked to side, number of cycles or IMC techniques: 44/62 had had mixed beam) versus good late survival. It has been shown that an optimal IMC technique (mixed beam) allowed a decrease in local relapse rate and survival (Cuzick*) with a low cardiac morbidity (Pierce*) [JCO 94, 112, 444–453].