Diagnosis, Treatment and Prognostic Factors in Breast Cancer

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ROLE OF COMBINATION ADJUVANT THERAPY FOR OPERABLE BREAST CANCER

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Previous studies have shown a benefit in terms of an increase in disease-free survival (dfs) for both tamoxifen and cyclophosphamide given post-operatively. The aim of the current study was firstly to repeat two of these trials, and secondly to assess any potential benefit of giving both drugs in combination.

A factorial design trial was used in which a total of 1912 patients with operable carcinoma of the breast were randomly assigned to one of four groups; neither drug, tamoxifen alone, cyclophosphamide alone or both tamoxifen and cyclophosphamide.

Assuming no interaction between the two treatments results of the current study show a 33% increase in dfs associated with tamoxifen (95% CI: 16% to 54%) and a 13% increase in dfs associated with cyclophosphamide (95% CI: 1% reduction to 22% increase).

We discuss both the implications of this study with respect to combination therapy, and the role of factorial designs for large, pragmatic phase III trials.

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NON PALPABLE BREAST LESIONS: ANALYSIS OF 952 OPERATED CASES.

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From 03.85 to 06.92, 952 patients with non palpable breast lesions were operated on our Institute.The mammographic findings consisted of cluster microcalcifications in 506 cases (53%),suspicious opacities in 318 cases (33%) and opacities within microcalcifications in 128 cases (13%). The histologic findings showed benign breast disease in 481 cases (50.5%), whereas in 471 (49.5%) a carcinoma was found. Intraductal component was present in 58 cases. Non infiltrating carcinomas were found in 124 cases (26.6%): 94 patients (75.8%) with intraductal carcinoma (DCIS). Conservative treatment was performed in 86% of cases with invasive cancer, and in 90% of DCIS patients. Frozen section was performed in 666 cases with 12.5% of discordance. 19% of invasive carcinomas had axillary lymph node involvement, but only 4 cases, with tumor size <=5 mm., showed axillary metastases and 18 had >3 metastatic nodes.

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INTENSIVE CHEMOTHERAPY WITH HIGH DOSE EPIRUBICIN (EPI) IN ADVANCED BREAST CANCER. THE EXPERIENCE OF THE HELLENIC CO-OPERATIVE ONCOLOGY GROUP (HeCOG)

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Preclinical as well as clinical studies suggest that anthracyclines have a steep dose-response curve in advanced breast cancer. Our group in a series of phase II studies has tested the activity and toxicity of high dose EPI (110 mg/m2) in pts with advanced breast cancer. In the first study (HE 1088), in which 52 pts were included, EPI was intented to be given every 3 weeks. Actually the median treatment interval was 26 days. Thus in the subsequent study (HE 1090) 42 patients were treated with the same dose of EPI but every 28 days with G-CSF support. In the third study (HE 1091), which included 50 pts, an attempt was made to improve the response rate by increasing the dose intensity (DI) of EPI. Therefore, the treatment interval was reduced to 14 days with G-CSF support also. The median drug dose actually received per patient in the above-mentioned studies was 76%, 100% and 99,9% of initially planned dose. Median DI of EPI was 29, 27 and 53 mg/m2/wk respectively. Response rates were 35%, 37% and 64% respectively. Grade 3-4 leukopenia was observed in 27%, 21% and 6% respectively and stomatitis in 14%, 0% and 4% respectively. In order to further explore the issue of DI of anthracyclines in advanced breast cancer, our group initiated last year a prospective randomized study where 110mg/m2 of EPI are administered with G-CSF every 4 or every 2 weeks. Quality of life is also measured by the LASA method.

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PHOTODYNAMIC THERAPY FOR SUPERFICIAL CUTANEOUS MAMMARY METASTASES USING PHOTOFRIN.

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Photodynamic therapy is a relatively new modality for the treatment of small localized tumors. It can be applied when other means of treatment have already failed, as in patients with skin metastases of mammary carcinoma. These patients are at risk for ulcerations, pain and suffer from psychological stress due to the physical recurrence of the disease. In the Netherlands Cancer Institute we have initiated a treatment protocol using Photofrin for patients with recurrent localized carcinoma in the skin. A low dose Photofrin (0.75 mg/kg) was given intravenously 2 to 5 days before illumination with light of 630 nm from an Argon Dye laser. Using a microlens, areas of 3 cm diameter (7 cm^2) of biopsy proven tumor were illuminated using a fluence rate of 150 mW/cm^2 and energies of 150-200 $Joules/cm^2$. Three patients have been entered in this study to date. Illumination with different energy doses indicated that 175 $Joules/cm^2$ gave optimal results with scab formation after 5 to 7 days and preservation of the normal skin tissue. Normal healing processes were observed after 6-8 weeks and biopsies were negative for residual tumor. The treatment was well tolerated by the patients and the major side effect of Photofrin, skin photosensitivity, lasted for only 14-20 days after this low photosensitizer dose.

Conclusion: These preliminary results indicate that PDT using low doses of Photofrin for superficial skin metastases is feasible with limited side effects but that the lesions to be treated must be restricted to a surface of approximately 100 cm and tumor invasion not beyond 5 mm.