

# Proffered papers

## Breast cancer — adjuvant therapy

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### RADIOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

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A review of 300 cases of locally advanced breast cancer, referred to the Instituto Português de Oncologia, Porto were studied from January, 1985 to December, 1988, to evaluate the therapeutic approach of Radiotherapy.

They were classified in two groups; the first one received Radiotherapy (52%) and the other one (48%) didn't.

Total survival and disease free survival curves were evaluated in relation to different parameters (hormonal state, histologic tumor grade, pathologic state, lymphnodes involvement, local recurrence and distant metastasis). Survival rates were calculated according to Kaplan-Meier's method and the differences between pairs of survival curves were assessed by the Logrank method. The significance level was  $P < 0.05$ .

A statistically significant improvement was observed in the group receiving Radiotherapy for most of the parameters ( $P < 0.0001$ ), showing the importance of this treatment in the approach of locally advanced breast cancer.

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### ERBB2 OVEREXPRESSION AFFECTS TAMOXIFEN EFFICACY IN THE ADJUVANT TREATMENT OF NODE NEGATIVE OPERABLE BREAST CANCER PATIENTS

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**Aim.** To study retrospectively the interaction between ErbB2 overexpression and adjuvant tamoxifen in node negative breast cancer patients (pts) entered into the controlled clinical trial GUN-1 (*Lancet* 1988, ii: 1095). **Patients and Methods.** ErbB2 was evaluated by immunohistochemistry in 150 out of 173 pts who had been randomly assigned to 2-year adjuvant tamoxifen (TM) (n. = 90) or no further therapy (n. = 60). ErbB2 was defined positive if more than 10% of cells showed specific membrane staining. **Results.** As of November 30, 1994, median follow up is 12 years. ErbB2 was overexpressed in 44/150 pts (29.3%). The addition of ErbB2 to a multivariate Cox model, containing age, menopausal status, tumor size, nuclear grade and treatment as covariates, was not statistically significant, while the addition of first order interaction between ErbB2 and TM was statistically significant both for DFS and OAS; the same result was obtained also when the basal model contained estrogen receptor (ER) and ER-TM interaction. Indeed, adjuvant tamoxifen significantly prolonged DFS ( $P = 0.0009$ ) and OAS ( $P = 0.03$ ) only among ErbB2 negative cases, while no difference was observed in ErbB2 positive cases both for DFS ( $P = 0.22$ ) and for OAS ( $P = 0.12$ ).

Dr. De Laurentiis is recipient of an AIRC fellowship.

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### UNEXPECTED OPPOSITE AGE RELATED EFFECT OF ADJUVANT HIGH-DOSE PROGESTERONE ACETATE (HD-MPA) FOR NODE POSITIVE (NP) EARLY BREAST CANCER: 10 YEARS RESULTS OF A MULTICENTER RANDOMIZED TRIAL

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281 NP early breast cancer patients among whom 270 were fully evaluable were randomized to receive either no hormonotherapy (group A) or an hormonotherapy with HD-MPA (500 mg IM daily for 4 weeks then 500 mg IM twice weekly for 5 months); all patients received also 6 monthly courses of IV CMF.

Patients characteristics were well balanced among both groups. The toxicity of chemotherapy was evaluated on 2960 courses. In HD-MPA arm irrespectively of age, patients could better tolerate CMF chemotherapy with less WBC, granulocyte, nausea-vomiting toxicities and infections, and higher dose-intensities ( $P 0.02-0.0001$ ) as well as higher dose intensity products ( $P 0.001-0.0001$ ). Relapse free survival (RFS) and overall survival (OS) were not different at the whole group level (at 10 years: 0.50 in both arms) or as regard T, number of positive nodes, receptor categories, type of surgery or radiotherapy. However a striking difference was observed when patients were split according to age ( $< 50$ ;  $\geq 50$ ) or menopausal status. If older patients benefited from the combined treatment (at 10 years RFS: A: 0.38; B: 0.54 -  $P 0.003$ ; OS: A: 0.52; B: 0.63 -  $P 0.11$ ), younger patients had a significantly worse prognosis when treated with CMF + HD-MPA, (at 10 years: RFS: A: 0.67; B: 0.45 -  $P < 0.01$ ; OS: A: 0.80; B: 0.53 -  $P < 0.009$ ).

**In conclusion:** in less than 50 years patients, HD-MPA had a negative adjuvant impact both on RFS and OS. These results contrast with the results obtained in older subjects and with the excellent adjuvant impact of HD-MPA observed in node negative early breast cancer patients. This observation warrants further randomized evaluation in  $< 50$  years NP subjects comparing chemotherapy alone versus sequential chemohormonotherapy.

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### SURGICAL COMPLICATIONS RELATED TO PERIOPERATIVE ADJUVANT CHEMOTHERAPY IN BREAST CANCER. RESULTS OF A PROSPECTIVE, CONTROLLED, RANDOMIZED CLINICAL TRIAL

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From May 1985 to June 1992, 375 patients (pts) were enrolled in a prospective controlled randomized clinical trial of periop adjuvant chemotherapy (PAC) associated to long-term adjuvant chemohormonotherapy in order to test the effectiveness of reducing the time interval between surgery and chemotherapy. Here, the short-term surgical complications related to PAC are reported in order to verify whether such treatment might negatively affect the results of breast cancer surgery. Pts undergoing PAC received within 48-72 hour following surgery one course of CY (600 mg/sqm), EPI (60 mg/sqm), and 5-FU (600 mg/sqm) (CEF); pN+ pts, who were given perioperative CEF, had five further cycles of CEF alternated with six cycles of CMF (CY 600 mg/sqm, MTX 40 mg/sqm, 5-FU 600 mg/sqm). All other pN+ pts had six cycles of CEF alternated with six cycles of CMF, starting within 30 days after surgery. No significant difference of postop morbidity was observed in the two groups as regards median hospital stay (8 days), number of outpatient dressings (3.5 vs 3), seroma (51 = 26.9% vs 45 = 24.2%), lymphatic drainage (400 vs 409 ml), and postop infections,