

121 P

HEPATOSTEATOSIS AND ALTERATIONS OF CA15.3 AND CEA IN PATIENTS WITH BREAST CANCER RECEIVING TAMOXIFEN

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The purpose of this report was to determine if ultrasonographically documented hepatic steatosis would alter the levels of serum CA15.3 and CEA in breast cancer-patients receiving tamoxifen. We measured serum CA15.3, CEA, AST, ALT, alkaline phosphatase, HDL and LDL levels in 51 patients with steatosis and in 68 without steatosis. Patients who had metastasis were excluded. One hundred ninety four CA15.3 and 193 CEA measurements for steatotic group and 154 CA15.3 and 184 CEA measurements for non-steatotic group were performed. Two times higher levels of CA15.3 and CEA were found to be more frequent in steatotic group (30% versus 14% and 53% versus 5%, respectively). Median duration of tamoxifen usage were longer in steatotic group (49 months versus 21 months). There were no significant differences in liver enzymes and lipid levels between steatotic and non-steatotic groups. We suggested that tamoxifen may be responsible for the ultrasonographically documented hepatic steatosis in patients with breast cancer.

123 P

BREAST AND COLO-RECTAL CANCER IN EUROPE: PROBLEMS RELATED TO COLLECTION AND ANALYSIS OF DIETARY DATA.

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Assessment of dietary intake is important in epidemiological studies of diet and cancer at many sites, but is crucial when considering cancer of the colon, rectum and breast. In the framework of the Collaborative, Multicentre, Case-Control Study of Breast Cancer and Colo-Rectal Cancer food frequency questionnaires (FFQs) and food composition databases (FDBs) were tailored specifically for the participating centres. Here problems and approaches in developing and validating FFQs and FDBs for the centres in Italy, Slovenia and Ireland will be described and comparison made of the resulting instruments. All FFQs are interviewer administered. The Italian FFQ includes 78 questions on the frequency of consumption of specific foods, or groups of foods, as well as additional questions on fat consumption. An ad hoc FDB including almost 2000 foods and dishes was developed for this study, mainly from data provided by the National Nutrition Institute of Rome. In Slovenia, the food frequency questionnaire was developed with a structure that is very similar to that of the Italian instrument. A total of 136 items, plus alcoholic beverages and coffee, are included in the questionnaire. In Ireland the final list of questions includes 176 foods, plus alcoholic beverages and coffee. The complete FDB includes approximately 3000 items and is mainly derived from the British food composition tables. The final versions will be a major resource for cancer research in these countries for many years.

125 P

BREAST CANCER PATIENTS GENERALIZED AT DIAGNOSIS HAVE A SIGNIFICANTLY BETTER RESPONSE TO POLYCHEMOTHERAPY THAN THOSE WITH RELAPSE AFTER CURATIVE SURGERY

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Neoadjuvant chemotherapy of breast cancer results in high response rates of > 85%. This demonstrates a high sensitivity of breast cancer cells to cytostatic treatment as first-line intervention. Since response rates in generalized disease are considerably lower (40-45% for anthracyclin-mono-therapy and 50-70% for polychemotherapy), we performed a matched-pair analysis to compare the response to first-line polychemo-therapy (FEC) of breast cancer patients generalized at diagnosis (group I, n=15) and patients with distant disease after surgery and > 1 year disease free interval (group II, n=35). Both groups were comparable in terms of age, hormone-receptor status, histological grading, pattern of metastasis, and menopausal status. No patient of group II had received anthracyclin-containing adjuvant therapy. We detected a significantly higher ($p < 0.01$) response rate (SD+PR+CR) in patients of group I (100%) vs. group II (68%) and significantly ($p < 0.1$) more patients of group I (92%) experienced objective remissions (PR+CR) than those of group II (56%). The possible impact of neoadjuvant chemotherapy on survival in patients with generalized disease at diagnosis remains to be determined. However, this data supports the rationale for neoadjuvant therapy to eliminate micro-metastasis early in the course of the disease and leads to trial conceptions which could include high-dose chemotherapy in the neoadjuvant setting in patients with high risk for relapse.

122 O

A PHASE I TRIAL OF EPIRUBICIN (E) AND PACLITAXEL (P) IN PATIENTS WITH METASTATIC BREAST CANCER (MBC).

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We have performed a phase I study in MBC patients (pts) to determine the maximum tolerated dose (MTD) of P to be administered in association with E at a fixed dose of 90 mg/sqm. P was given i.v. by a 3 hrs infusion, immediately after E, starting from a dose of 135 mg/sqm and escalating by 20 mg/sqm for each dose level until DLT. DLT was defined as follows: absolute neutrophil count (ANC) <500 uL for >7 days or <100 uL for >3 days, febrile neutropenia or any G3 non hematologic toxicity. G-CSF was allowed to accelerate recovery of G4 neutropenia lasting more than 3 days. An Holter EKG was performed at each course and the left ventricular ejection fraction (EF) was evaluated every 2 courses by echo-doppler. 32 patients with the following characteristics have been treated: median age 54 (30-66) yrs; median (ECOG) PS 0 (0-1); 84% of the patients had failed adjuvant chemotherapy (including anthracycline in 14 cases). The dominant metastatic sites were: viscera 20 pts (62%), soft tissue 11 pts (34%), and bone 1 pts (3%). The DLT is febrile neutropenia which occurred at the first course in 2/8 pts patients treated with P 225 mg/sqm. A total of 176 courses have been administered; a G4 neutropenia occurred in 66% of the courses, lasting a median of 4 days (range 1-8). G-CSF (300 ug/kg/die) was given in 34% of the courses for a median of 5 days (range 2-12). Most significant non hematologic toxicities were: a G 1-2 mucositis in 29% of the courses and a G 1-2 peripheral neuropathy in 56% of the pts. The cardiac toxicity was low: only 2 pts showed a drop of the EF below 50% after 6 courses; no sign of congestive heart failure was observed. The overall response rate is: 76% with 14% of complete responses (95% C.I. 56-90%). In conclusion we have demonstrated that the combination of E and P is feasible, devoid of cardiac toxicity and active in a population of pts who failed adjuvant chemotherapy. Our recommended phase II dose of P is 200 mg/sqm.

124 O

DOES TIMING OF SURGERY FOR BREAST CANCER AFFECT PROGNOSIS?

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It has been claimed that premenopausal women with breast cancer have worse prognosis if the surgery is performed during the follicular phase of the menstrual cycle (days 3-12.) compared to other days. Previous studies on this subject have relayed on clinical data for placing women in the menstrual cycle. We wanted to estimate the accuracy of that, and study the relationship between the hormonal profile and prognosis.

Blood samples were taken at the day of surgery from all women diagnosed from 1988-90, younger than 55 years old, and registered at the Icelandic Cancer Registry. Diagnosed women were 106, but eligible were 66 women. Clinical data and hormonal measurements were collected. The follow-up time was on average 32 months.

Women who had surgery during the follicular phase had less overall survival ($p=0,03$). High testosterone level was a profound prognostic marker in a multivariate analysis (RR=6,7). Inconsistency was in placing the women in the menstrual cycle, i.e. 30% of the women who were in follicular phase according to hormonal profile were expected to be on other days of the menstrual cycle according to clinical data.

126 P

RELATIONSHIPS BETWEEN THE TIME OF OCCURRENCE OF PULMONARY METASTASES AND THE VOLUME OF PRIMARY TUMOUR IN BREAST CANCER.

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Although a primary tumour of breast cancer can be detected at the size of 1-3 cm³ a significant proportion of patients refer to the physician when a tumour is even 10³ times larger. Pulmonary metastases, in regularly followed-up patients, are detected at similar sizes, when the largest tumour, or a pleural fluid become visible on chest x-ray. Assuming a constant, exponential growth rate of primary tumour and metastases the differences in time of occurrence of pulmonary metastases will depend upon the differences in volume of primary tumour at the time of diagnosis and upon the volume doubling time of primary tumour. Data of 112 patients with breast cancer who developed pulmonary metastases during the course of disease were analysed basing on this model. It was shown that the median growth rate of pulmonary metastases developed from small primary tumours was higher than the growth rate of metastases developed from large primary tumours. Volume doubling times of primary tumours were calculated: 220 days for operated tumours and 49 days for tumours detected in advanced, inoperable stage.