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Accumulation of p53 is associated with response to pre-operative chemotherapy in primary operable breast cancer

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Material from breast cancer patients treated with pre-operative chemotherapy offers the possibility to directly gauge response of the primary tumor and correlate this response with various tumor characteristics. Chemotherapy acts at least in part by inducing apoptosis in tumor cells. We investigated the predictive value of two important regulators of apoptosis, Bcl-2 and p53, as well as a number of clinico-pathological parameters using tumor material from 178 patients treated with pre-operative chemotherapy in EORTC Trial 10902. these patients were randomized to receive four courses of pre-operative chemotherapy (5-FU, Adriamycin, Cyclophosphamide) followed by surgery. Mammograms were made before the first and following the last course of chemotherapy. Tumor response was assessed in two ways, using either clinical or mammographical measurements. P53 accumulation and Bcl-2 and estrogen receptor expression in core needle biopsy material was determined with the use of immunohistochemistry. 25.4% (28/110) of evaluable tumor biopsies showed p53 protein accumulation (p53-positive tumors). 89.3% (25/28) of these p53-positive tumors showed a clinical response (complete or partial response) to chemotherapy ($p < 0.001$). In addition, 73.7% (14/19) of these tumors showed a significant reduction in mammographical density, suggesting treatment response. However, no significant association was found between p53 accumulation and changes in either clinical or mammographical tumor size. Bcl-2 expression, estrogen receptor status, patient age, tumor-size, node-status and multicentricity were not significantly associated with responsiveness.

Conclusion: the presence of mutated p53 seems to be associated with chemosensitivity in primary breast tumors.

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PS2 helps to predict responders to tamoxifen therapy in patients with recurrent breast cancer

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Background: Levels of oestrogen (ER) and progesterone receptor (PgR) in primary breast carcinoma indicate those patients likely to benefit from tamoxifen therapy. PS2, an oestrogen-inducible protein, has been suggested as an additional marker for a favourable response.

Purpose: Our aim was to investigate PS2 as a marker of response and progression free survival in a large series of patients.

Methods: ER, PgR and PS2 were determined in cytosols of 764 primary breast tumors. All patients were treated with first line hormonal therapy for systemic disease. They received tamoxifen 40 mg/day. Median follow-up of patients alive was 93 months and 36 months after start of therapy.

Results: One hundred and twenty-nine patients (17%) were objective responders, 286 (37%) showed stable disease, the remaining 349 (45%) patients had progressive disease within 6 months. In univariate analysis age, disease free interval, site of metastasis, ER, and PgR were significant for both response and time to progression. PS2, corrected for these variables, was an independent predictive factor in the multivariable models.

Conclusion: PS2 level of the primary tumor helps to predict responders to first line tamoxifen treatment for recurrent breast cancer.

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Wednesday, 30 September 1998 16:00-18:00

EUROPA DONNA SYMPOSIUM

Life style and diet – their influence on breast cancer

137 INVITED

Current trends in breast cancer

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Abstract not received.

138 INVITED

The patient role in healing

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Abstract not received.

139 INVITED

Dietary factors and breast cancer

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The role of diet, particularly fat intake, in breast cancer is one of the most controversial and difficult areas, due partly to interlocking effects of fat on obesity, age at menarche, and serum oestrogen levels, which, together with differences in childbearing practices and use of exogenous hormones affect lifetime exposure to oestrogens.

Case control studies indicate that women who develop postmenopausal breast cancer report having eaten more fat than their healthy counterparts, but later reports from prospective studies have not supported a role for fat in reducing risk, at least in adult life. Diet in adolescence or earlier may influence age of menarche and later breast cancer risk and other dietary factors, in addition to high levels of body fatness, hasten the onset of menarche. Obesity is associated with an increased risk of postmenopausal but not premenopausal breast cancer. Alcohol increases risk and new evidence shows that meat, rather than fat, seems to be better associated with breast cancer risk, particularly red and fried meat.

Other factors in plants that affect hormonal status and perhaps risk of breast cancer are non starch polysaccharides and the phytoestrogens, which are chemically similar to oestradiol. Genistein, has many other anti-cancer effects unrelated to its antioestrogenic role, although an oestrogenic effect on the breast cannot be ruled out at present.

140 INVITED

Psychological factors in the use of complementary therapies

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The immediate crisis of hearing the diagnosis of cancer and the long-term psychosocial effects of this diagnosis are discussed from a psychodynamic point of view. The cognitive and behavioural aspects of coping with the stress are considered, with particular reference to the use of complementary therapies.

Shifts of attitude and perception which lead to the taking of a more active role in fighting the tumour are part of the decision to begin and to continue using complementary therapies. The psychodynamics of hope are elaborated – hope of at least a better quality of life thanks to complementary therapies, and possibly also an extension of life.