tissues from Japanese women. In a part of them, normal breast tissues were analyzed concomitantly. ERa was positive in 81.8% and 77.3% of primary cancers for exon 5 and 7, respectively, and ERb was positive in 54.5%. Among 49 positive for both exons of ERa, 26 were positive and 23 were negative for ERb. Among 8 negative for both exons, respective 4 were positive and negative for ER b. Thus no correlation was observed between expression of ERa and ERb in cancer tissues. While all 8 of normal breast tissues expressed ERa, ERb was positive in only 5 of them. The expression of ERb in normal tissues did not coincided with that in cancer tissues from same breast. The expression (i.e.; function) regulations of ERa and ERb in human breast tissues, therefore, seemed to be mediated by different mechanisms irrespective of their pathological characteristics.

381   ORAL

Urokinase-like plasminogenactivator (uPA) and plasminogenactivator-inhibitor type 1 (PAI-1) in primary breast cancer – Predictive markers for tamoxifen resistance?

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Estrogen and progesterone receptor status are established predictive factors for response to endocrine treatment in the adjuvant and palliative situation. Overexpression of the new prognostic factors uPA and PAI-1 have been reported to be predictive of resistance to Tamoxifen in metastatic disease.

We evaluated from our data the impact of uPA and PAI-1 on hormonal treatment. uPA and PAI-1 were determined out of fresh tumor specimens using a commercially available assay (Immunobind®-ELISA from American Diagnostica). 178 patients with primary breast cancer stage I, II or III received endocrine treatment with Tamoxifen 30 mg. Decision about treatment was not influenced by knowledge of uPA or PAI-1. Median follow-up was 27 months. Statistic analysis was done by Kaplan-Meier-estimates for survival data and Mann-Whitney-Test for cross-checks of distribution. Multivariate analysis was performed with the Cox-Regresion-Model.

Overexpression of uPA (>3.0 ng/mg protein) was present in 49%, overexpression of PAI-1 (>14.0 ng/mg protein) in 41% of all cases. Overexpression of uPA and PAI-1 was significantly correlated with higher nuclear grading (p = 0.02) and overexpression of PAI-1 with lower estrogen receptor expression (p = 0.01). Age, progesterone receptor expression, tumor stage, nodal stage were equally distributed between tumors with or without overexpression. Recurrence free survival (DFS) was 53 months for patients with uPA-overexpression versus 49 month in the control group (p > 0.05, n.s.), for patients with or without PAI-1 overexpression DFS was 51 months (p > 0.05, n.s.). Multivariate analysis for DFS and overall survival revealed only number of positive lymphnodes as predictive factor for recurrence or death

In this study endocrine treated patients in the adjuvant situation with overexpression of uPA or PAI-1 had no worse prognosis than patients without overexpression. uPA and PAI-1 overexpression were not predictive for Tamoxifen-resistance.

382   ORAL

Hormone replacement therapy does not influence pathological stage of breast cancer in 1113 tumours

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Women using Hormone Replacement Therapy (HRT) at diagnosis of breast cancer have been reported to have smaller more node negative tumours of better grade and to have lower mortality than non users. We have shown that significantly more women using HRT when they were screened developed interval cancers compared to non users. It is therefore important to include interval cancers in any study of the possible HRT effect on tumour type, size, grade and nodal status.

1113 women aged between 50 and 65 years were screened between 1988 and 1993 and either had a screen detected cancer (SDC) (816 women) or developed an interval cancer (297 women) up to the end of 1996. Current HRT usage was recorded at the time of screening and also at presentation with breast cancer. Of the 816 women with SDC 100 (12.3%) were using HRT when they were screened. Of the 297 women who developed interval cancers 66 (22.2%) were currently taking HRT at diagnosis. Of the 1113 women studied therefore 166 women (15%) were HRT users when they developed breast cancer. There were no significant differences in the type, size or grade of tumours or nodal status comparing HRT users with non

users. These results do not support the commonly held belief that HRT users develop tumours with favourable prognostic features.

383   POSTER

Women taking hormone replacement therapy develop low grade tumours

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Women taking hormone replacement therapy (HRT) are said to have a higher risk of developing breast cancer but the tumours they develop may be of a lower grade. In order to remove any bias introduced by pre-existing subclinical tumours, the impact of HRT on the development of breast cancer was assessed by studying women who had cancers detected at routine screening mammography subsequent to normal mammograms.

372 women had such tumours detected between 1.1.91 and 1.7.97. Patients who went on to have treatment outside the region (59) were excluded from the study.

Data regarding brand of HRT, dose and duration of use was collected along with details of tumour pathology such as size, grade, lymph node status and presence of carcinoma in situ (CIS). Women who had previously taken HRT but had stopped were excluded, then women who were taking HRT at the time of diagnosis (80) were compared with those who had never taken HRT (202).

Overall, women on HRT were found to have lower grade tumours than those not taking HRT, p = 0.05 X2 test, and women with lower grade tumours had been taking HRT for longer, grade 1 = 72 months ± 74.3, grade 2 = 53 ± 36.7, grade 3 = 40 months ± 32.8. There was no relationship between HRT use and tumour size (users 13.59 mm ± 8.22, non-users 15.95 mm ± 9.95), lymph node positivity, or CIS, although there was a trend in women taking HRT to have CIS around the tumour.

In conclusion, tumours which develop in women taking HRT are more likely to be of a lower grade and may be associated with carcinoma in situ.

384   POSTER

Change in expression of ER and BCL-2 predict for quality and duration of response in endocrine sensitive breast cancer

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Aims: Pre-treatment oestrogen receptor (ER) status in human breast cancer is correlated with sensitivity to first-line endocrine therapy but is not accurate enough to predict for quality or duration of response. We have previously shown that ER expression is down-regulated during anti-oestrogen treatment. This study has investigated whether the degree of change in expression of ER and related biological markers determines for quality and duration of endocrine response.

Methods: 125 patients (61 Stage I–II elderly, 54 Stage III, 10 Stage IV) underwent sequential tumour biopsies at diagnosis, 6 weeks and 6 months for immunocytochemical assessment of ER, PgR, pS2 and bcl-2 expression whilst on primary tamoxifen. Response at 6 months was assessed by UICC criteria. 22 patients showed de novo resistance, 53 achieved static disease (SD), 43 partial response (PR) and 7 complete response (CR). Median follow-up is 46 months.

Results: Objective responders (OR) had significantly longer duration of response (DofR) than SDs (p = .0016). Greater % fall in ER H-score between pre-treatment level and both 6 weeks (p = .035) and 6 months (p = .046) was significantly associated with better quality of response (OR vs SD). Greater % reduction in bcl-2 H-score (p = .038) and ER H-score (p = .029) at 6 weeks were significantly correlated with longer DofR. The sub-set of ORs displaying greatest fall in ER H-score at 6 weeks (n = 17) achieved longest DofR of all responders (p = .008).

Conclusion: We believe this to be the first study to demonstrate that degree of change in expression of ER and the related biological marker bcl-2 predict for quality and duration of response in endocrine sensitive breast cancer.