O-1. HORMONE RECEPTOR STATUS IN PRIMARY BREAST CANCER – TIME FOR A CONSENSUS?

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Aim: In a previous study, we demonstrated wide variability in access to oestrogen receptor (ER) measurement, patient selection, choice of technique and cut-off point for positivity. The aim of this study was to determine current status of ER and progesterone receptor (PR) measurement in the UK.

Methods: A postal questionnaire was sent to the lead breast surgeon of all 229 Breast Cancer Units in the United Kingdom listed in the 1999 Macmillan Directory of Breast Cancer Services. The surgeons were asked about availability, use and technique of ER and PR measurement in their units. These results were compared with the previous study carried out in 1997.

Results: Questionnaires were returned from 170 (74%) units in the UK. Of these 99% stated measurement of ER status was important in the management of their patients, an increase of 12.5% from the previous study. Access to ER measurement was now available in 100% of units although this facility was off-site in 21%. ER status was determined on all new breast cancers in 84% of units while the remaining 16% used a selective policy. The majority of units used an immunocytochemical technique (85%).

ER positivity was determined using either the percentage of cells staining positive (33%) or in combination with the intensity of staining (44%). In the former group the absolute cut-off for positivity varied widely from 5–80% of cells.

Of the 229 units, 107 (63%) felt that PR measurement was important.

Discussion: This study confirms considerable variability in both the technique of ER measurement and the absolute cut-off point for positivity (5–80%). Since ER status strongly influences the choice of adjuvant therapy, as well as accrual into clinical trials, it is essential that a consensus is reached regarding the choice of technique as well as the threshold for positivity.

O-2. THE RELATIONSHIP OF OESTROGEN RECEPTOR (ER) STATUS TO TREATMENT OUTCOME IN BREAST CANCER (BC) THERAPY

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The value of ER status as a predictive factor for response in BC is well known. The endocrine agents, tamoxifen (TAM), goserelin (GOS) and anastrozole (AN) have all been used successfully in the treatment of different stages of BC. We review the importance of ER status with respect to efficacy of TAM, GOS and AN. The most recent publication from the Early Breast Cancer Trialists Collaborative Group (EBCTCG, 1998), on adjuvant TAM, which to date includes a total of 37,000 pre- and postmenopausal patients (pts), showed that the reduction in disease recurrence resulting from 1, 2 and 5 years of TAM treatment was 21%, 29% and 47%, respectively, in pts with ER-positive tumours, but the reduction in disease recurrence was much less in pts with ER-negative tumours. Similarly, 1, 2 and 5 years of TAM treatment produced proportional mortality reductions of 12%, 17% and 26%, respectively, in pts with ER-positive tumours while the overall mortality reduction was only 6% in pts with ER-negative tumours. In peri- and premenopausal pts with early BC randomized to GOS (3.6 mg monthly, n = 817) or cytotoxic chemotherapy (CMF, six cycles, n = 823) a highly significant interaction between treatment and ER status (p = 0.0016) was observed and therefore protocolled ER subgroups were analysed separately. In pts with ER-positive tumours (73.7%, n = 602/817), GOS was equivalent to CMF with respect to disease-free survival (DFS) (hazard ratio [HR] = 1.01; 95% confidence interval [CI] = 0.84–1.20). In pts with ER-negative tumours (18.8%, n = 154/817), CMF was superior to GOS with respect to DFS (HR = 1.76; 95% CI = 1.27–2.44). The large multicentre, randomised, double-blind TARGET study, where 44.6% (n = 297/668) of pts had ER and/or progesterone (PR) (ER/PR) positive tumours showed that AN (1 mg daily) was equivalent to TAM (20 mg daily) in terms of time to disease progression (TTP) (8.2 vs 8.3 months). However, results of the identically designed North American study, where 88.4% (n = 312/353) of pts had ER/PR positive tumours showed a significant increase in TTP by 5.5 months in TTP in the AN arm (HR = 1.44, lower 1-sided 95% confidence limit = 1.16, p = 0.005). This result was further supported in a study of 238 PM pts with ER positive tumours, in which the TTP was increased 7.3 months in the AN arm (HR = 0.77, 95% CI = 0.61–0.82, p = 0.047). These recent examples clearly highlight the importance of ER assessments before initiation of BC treatment.

O-3. HYPOTHESIS P53 MUTATION AS BASIS FOR EFFECT OF PACLITAXEL-CONTAINING THERAPY ON ER-NEGATIVE TUMOURS AND OF TAMOXIFEN IN OBFUSCATING THIS IN ER-POSITIVE IN CALGB9344

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Since the 30-month median follow-up analysis of the CALGB 9344 study, the lack of an obvious biological hypothesis to explain the striking sensitivity of ER-poor tumours to paclitaxel, and insensitivity of ER-positive (pos) has caused some concern. We advance here a simple and plausible candidate explanation.

ER-negativity has long been appreciated as a poor prognostic factor. Chemotherapy represents the only form of effective systemic adjuvant therapy for patients with ER-negative (neg) tumours. A subset of these contain mutant or null p53 and these tumours are often resistant to conventional drugs. Such mutations are more frequently found in ER-neg tumours than ER-pos (p = 0.01), although P53 over-expression has also been significantly linked to higher histological grade (p = 0.001) and increased tumour size (p = 0.02). Some analyses have shown that p53 mu-