Result: Fluorescence colorization were noticed on breast cancer cells. Besides it is easy to differentiate lymphocytes from cells of positive telomerase activity by way of morphology and color differences.

Conclusion: It is suggested that in situ TRAP method combined with cytologic diagnosis makes a great contribution to the improvement of diagnostic accuracy and the decrease of judged difference among persons and institutions.

Thursday, 1 October 1998 16:00-18:00

PARALLEL SESSION

Endocrinology

376 INVITED

Update on endocrine approaches in the treatment and prevention of breast cancer

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During the last 100 years endocrine procedures and agents became more and more important in the treatment and prevention of breast cancer.

The choice of endocrine drugs depends on the stage of disease, menopausal-status of the women, steroid hormone-receptors, and the toxicity profile of the drug.

In metastatic breast cancer patients endocrine therapy was the first effective palliative treatment and is also today's treatment of choice for low risk situation.

Along with adjuvant (post-operative) endocrine treatment with or without cytotoxic drugs it has been shown to improve disease-free and overall survival rates of primary breast cancer patients.

Neoadjuvant (primary or pre-operative) endocrine treatment is currently under investigation in the elderly patients to achieve more breast conserving surgery and better survival rates. Contrary to cytotoxic treatment endocrine therapy is active on tumor cells through distinct and highly selective mechanisms.

In the future endocrine treatment (e.g. tamoxifen, raloxifen, SERMS) will also play a major role for the prevention of breast cancer.

377 ORAL

Increased risk of recurrence for patients with EGFR and HER-p185 positive tumours when treated adjuvantly with tamoxifen for one year

A. Knoop[1], S. Bentzen[2], M. Nielsen[1], B. Rasmussen[3], C. Rose[1]. [1]*Dept. of Oncology, University Hospital, Odense;* [2]*Dept. of Experimental Clinical Oncology, University Hospital, Aarhus;* [3]*Dept. of Pathology Roskilde County Hospital, Denmark*

Aim: The aim of this study was to investigate interactions between treatment with tamoxifen and steroid receptor content and EGFR, HER-p185 and p53.

Methods: 1,716 high-risk postmenopausal breast cancer patients, who were all treated with irradiation, were randomly assigned to treatment with tamoxifen (868 women) or observation (848 women). The contents of the steroid receptors and expression of p53, EGFR, and HER-p185, were determined by immunohistochemistry. The follow-up time was 10 years. The endpoint was disease-free survival.

Results: Multivariate analysis demonstrated independent risk of disease for EGFR and HER-p185 positive high-risk patients and a decreased risk of disease in steroid receptor positive patients or patients with many positive lymph nodes when treated with tamoxifen. Patients with p53 positive tumours had an increased risk of disease, independent of adjuvant treatment with tamoxifen.

Conclusion: In patients with tumours positive for HER-p185 or EGFR another treatment than tamoxifen could be considered.

378 ORAL

Idoxifene antagonism of oestradiol-dependent MCF-7 breast cancer xenograft growth

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Purpose: Idoxifene is a novel selective oestrogen receptor modulator (SERM). We have previously shown idoxifene to have significantly greater inhibition of ER+ve MCF-7 xenograft growth in comparison with tamoxifen (TAM) when given in the absence of oestradiol (E2), (Br J Cancer 1997 75; 804–809). In our current study we compared the antagonist effects of idoxifene with TAM in MCF-7 xenografts whose growth continued to be supported with E2. In addition, we compared the activities of the cis and trans forms of idoxifene. Cis-idoxifene has a 50-fold lower relative binding affinity (RBA 0.25) for ER than either trans-idoxifene (RBA 12.5) or TAM (RBA 5).

Methods: 95 tumours were established with E2 support in ovariectomised athymic mice and after 4 weeks were randomised to either continued E2, cis-idoxifene + E2, trans-idoxifene + E2, TAM + E2, or withdrawal of E2. Drugs were delivered in equimolar doses by implanted silastic capsule changed every 8 weeks.

Results: Tumour growth continued with E2 and regressed exponentially upon E2 withdrawal, confirming the hormone-dependence of this model. Cis-idoxifene had no effect on E2-dependent tumour growth. In contrast, both trans-idoxifene and TAM significantly inhibited E2 dependent growth ($p < 0.0001$), and tumour volumes remained static over the subsequent 12 weeks of the experiment. Uterine weights in animals treated with either transidoxifene + E2, or TAM + E2 were significantly ($p < 0.009$) less than those treated with E2 alone.

Conclusions: These data show that idoxifene and TAM are equivalent in their ability to antagonise E2-dependent MCF-7 xenograft growth and therefore support the potential clinical utility of idoxifene in the treatment of breast cancer. Furthermore, these studies suggest that idoxifene's antagonist activity on tumour growth correlates well with its binding affinity for ER.

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379 ORAL

Ocular toxicity from standard dose adjuvant tamoxifen therapy

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Purpose: Ocular toxicity due to Tamoxifen is a recognised side effect of the drug, but few studies have attempted to discover how common the problem is. The literature shows that most reports are in the form of individual case studies of symptomatic patients, whilst cross-sectional studies have used relatively small sample sizes, with a wide variability in incidence found (0–12%). This study was undertaken to determine the incidence of ocular toxicity in patients on standard dose adjuvant Tamoxifen therapy for breast cancer.

Methods: 840 patients have been examined for signs of characteristic keratopathy/retinopathy. Many aspects of visual function were assessed, including visual acuities and central visual fields.

Results: Ocular toxicity was found in 6.7% of patients: keratopathy in 3.7% and retinopathy in 3.0%. Visual function was affected in 22% of those cases. The cumulative dose required for ocular toxicity to occur varied from 3.6 to 75g, suggesting that the problem is not simply dose related.

Conclusion: It was found that signs of ocular toxicity can be seen in asymptomatic patients with good vision, suggesting the need for regular ocular examination in all patients on Tamoxifen. The evidence does not indicate the need to discontinue the drug, unless a reduction in visual function is found.

380 ORAL

Estrogen receptor α and β expression in human breast cancer tissues analysed by RT-PCR

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The details of correlation between estrogen receptor α (ERa) and β (ERb) expression in human breast cancers have not been clarified yet. We analyzed expression of both receptors by RT-PCR on 66 primary breast cancer