or together with either trilostane (10 μM) or OHT (1 μM) for 72 hours. Cy5 or Cy3 fluorescently-labelled cRNAs were synthesised from experimental RNA samples and hybridised with oligonucleotide microarrays. Red (Cy5) or green (Cy3) fluorescence was analysed and treatment comparisons were performed.

In the presence of oestrogen, trilostane and tamoxifen had different actions on the expression of key sets of genes, including those coding for cell adhesion molecules, cell cycle and growth factor pathway components, and matrix-related proteins. Of particular interest was the preferential up-regulation of ER beta isoforms by trilostane. ER beta is thought to be down-regulated in tamoxifen-resistant tumours and is also a negative modulator of oestrogen's actions in both ERE- and API-dependent transcription. Therefore, this observation may provide an explanation for the clinical benefit seen with trilostane in patients who have relapsed on tamoxifen.

O-74. Caveolin-l expression in Tamoxifen-sensitive and resistant MCF-7 breast cancer cells

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We have previously shown that growth of a tamoxifen-resistant MCF-7 breast cancer cell line (Tam-R) is mediated by the epidermal growth factor receptor (EGFR)/mitogen-activated protein kinase (MAPK) signalling pathway. Components of this signalling pathway are found within caveolae as a result of binding to the principal coat protein, caveolin-l. Recent evidence suggests a reciprocal negative regulation exists between caveolin-l expression and EGFR/MAPK signalling activity and that hyperactivation of the MAPK pathway, as a result of caveolin-l downregulation, can drive cell transformation. To investigate whether caveolin-l plays a role in the development of tamoxifen resistance we have studied the relationship between caveolin-l and the oestrogen receptor (ER) and EGFR/MAPK signalling pathways in tamoxifen-sensitive (WT) and -resistant (Tam-R) MCF-7 breast cancer cell lines. RT-PCR, Western blotting and Immunocytochemistry were used to assess caveolin-l expression prior to and following pharmacological manipulation of ER and EGFR/MAPK pathways. An inducible caveolin-l expression system was used to evaluate the effects of caveolin-l expression in Tam-R cells. Caveolin-l mRNA and protein was expressed in WT, But not Tam-R cells. In WT cells, inhibition of ER up-regulated caveolin-l expression and reduced cell growth, whereas, blockade of EGFR activity increased caveolin-l expression but had little effect on proliferation. Blockade of EGFR/MAPK signalling similarly up-regulated caveolin-l expression in Tam-R cells. However, increased caveolin-l expression in both WT and Tam-R cells had no effect on EGF-induced activation of the MAPK pathway. These findings suggest a negative regulatory role for EGFR/MAPK signalling on caveolin-l expression but no reciprocal regulation of this pathway by caveolin-l in WT and Tam-R cells. Thus, caveolin-l appears to play no significant role in the development of tamoxifen resistance in this cell line.

O-75. Expressions of Cyclin B1 and CKS2 in breast cancers go down after short-term treatment with aromatase inhibitors

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Introduction: Changes in gene expression following short-term treatment may be helpful in identifying markers of tumor response to treatment. The aim of this study was to quantify changes in gene expression during treatment with aromatase inhibitors (AIs).

Materials and Methods: 21 post-menopausal breast cancer patients with estrogen receptor positive operable primary breast cancers received either letrozole or anastrozole for 14 days prior to surgery. Tumour samples were available before and after treatment. mRNA for mammaglobins 1 and 2 (MGB1 and MGB2), Cyclin-B1 (CB1), CDC28 pk 2 regulatory sub-unit (CKS2), Pleiotrophin (Ptph) and Lipin-2 (Lip2) were measured by real time PCR. 2-fold changes were regarded as meaningful.

Results: Results are summarized in the table.

	MGB1	MGB2	CB1	CKS2	Ptph	Lip2
Up	7	6	1	1	9	2
Stable	7	7	12	9	9	19
Down	7	6	8	11	3	0

Changes in MGB1 positively correlated with those in MGB2 ($p < 0.01$); similarly, CKS2 with Cyclin-B1 ($p < O.O1$).

Conclusion: Early changes in mRNA expression with treatment could be detected in all studied genes except for Lip2. Consistent changes were detected in CB1 and CKS2L, which were concordantly decreased in about a half of the studied cases. As these genes closely interact in promoting of cell cycle progression it is suggested that their dynamic measurements may be markers of early response to AIs in estrogen receptor positive postmenopausal breast cancer patients.

O-76. Does oestrogen receptor β expression influence survival in breast cancer?

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Background: Whilst it is ERα that is used routinely in assessment of breast cancer patient oestrogen receptor status, studies are now suggesting expression of ERβ to be also of great importance for therapy assessment. There is also a suggestion that ERβ levels may have greater influence in the biological behaviour of breast cancer, where the levels of ERα are low.

Methods: Archival formalin fixed paraffin embedded tissue was used from a group of 199 patients from 1996. There were three surgeons. The major difference in clinical practice was that two treated patients with neoadjuvant endocrine therapy (20 mg daily Tamoxifen 3 weeks pre-operatively) and other did not. All treatment was based on multidisciplinary meetings following national guidelines. Long-term survival was collected using the hospital breast cancer Database and used as end point.