information on the risk of recurrence was 'about right', 50.6% 'too little' and 0.6% 'too much'. 98 (53.8%) remembered being told this risk and 150 (82.4%) gave their own estimates. Patients' estimates and their expectations of the benefits of chemotherapy were compared with their actual risk as determined by the Early Breast Cancer Trialists' Collaborative Group overview.

Age	Nodal status	Est. % risk of rec. without chemo at 5 y (median)	Actual risk of rec. without chemo at 5 y	Est % risk of rec. with chemo at 5 y (median)	Actual risk of rec with chemo at 5 y
<50 y	Node −ve	50	34.1	15	24.7
N = 100	Node +ve	60	58.1	20	42.9
50–69 y	Node −ve	42.5	29.7	12.5	23.4
N = 50	Node +ve	62.5	46.7	20	40

When asked what degree of benefit they felt would make chemotherapy worthwhile, 71.1% of respondents would accept a reduction in the risk of recurrence at 5 y of ≤5%, (range 0.5 to 60%). In conclusion many patients overestimated both the baseline risk of recurrence and the potential benefit of chemotherapy. However, the majority would be prepared to accept similar treatment again for relatively modest benefit.

O-80. LIPSOME-ENCAPSULATED DOXORUBICIN (MYOCET) AND CYCLOPHOSPHAMIDE IS SUPERIOR TO EPIRUBICIN AND CYCLOPHOSPHAMIDE IN FIRST-LINE THERAPY OF METASTATIC BREAST CANCER

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We compared the efficacy and toxicity of liposome-encapsulated doxorubicin (Myocet) and epirubicin (EPI) when used in combination with cyclophosphamide (CPA) in first-line treatment of metastatic breast cancer (Metastatic Breast Cancer). 160 patients with Metastatic Breast Cancer and no prior anthracycline therapy were randomised to receive either Myocet (75 mg/m2) or EPI (75 mg/m2), in combination with CPA (600 mg/m2), every 3 weeks for a maximum of 8 cycles. The primary efficacy endpoints were response rate and time to progression. Responses were assessed by WHO criteria. Cardiac function was monitored by echocardiography. Median age was 54 in both treatment groups. Other prognostic factors were also balanced. Efficacy comparison showed superiority in favour of the MC combination. Overall response rate was 46% versus 39%, median time to disease progression was 7.7 versus 5.6 months (p = 0.02); median duration of response was 10 months versus 7.7 months (p = 0.005, median time to treatment failure was 5.7 months versus 4.4 months (p = 0.007). Mucositis was more common in patients who received the MC combination (grade 3: 7% versus 0% with EC). Cardiotoxicity was low in both treatment groups with no clinical. Heart failure reported it is of interest that was no grade 3/4 dermatitis reported with this liposome-encapsulated doxorubicin.

In this randomised prospective study, Myocet was superior to EPI in terms of time to disease progression when combined with CPA, but EPI may have had less acute toxicity in terms of stomatitis/mucositis.

O-81. CAPECITABINE NAMED PATIENT PROGRAM FOR PATIENTS WITH ADVANCED BREAST CANCER: THE UK EXPERIENCE

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102 patients with advanced breast cancer received capecitabine in a UK open access program and have been analyzed for response and toxicity. Median age was 53.2 (range 30–95). Patients had received between 0–4 prior chemotherapy regimens for advanced disease. 58% of patients had visceral disease and median number of sites of disease was 1. 60.8% had previously received anthracyclines, 25.5% taxoids and 6.9% infusional 5-FU. A median of 5 cycles were given.

Dose reductions occurred in 32.4% of patients (10.2% of cycles). The mean dose intensity was 95%. There were 3 complete responders, 17 partial responders, and the total objective response rate was 19%. Stable disease was achieved in 46% and progression was seen in 30%. Toxicity is tabulated.

Event	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Neutropenia	2.0	1.0	2.0	1.0
Thrombocytopenia	3.9	2.0	1.0	0.0
Mucositis	1.0	2.9	2.0	0.0
Fatigue	12.7	3.9	2.9	1.0
PPE	15.7	11.8	7.8	0.0
Diarrhea	21.6	5.9	4.9	2.0
Nausea	23.5	5.9	1.0	0.0
Vomiting	11.8	2.9	2.0	0.0

We conclude that capecitabine was well tolerated and active in extensively pretreated patients with advanced breast cancer. Toxicity was manageable at the recommended dose of 1,250 mg/m^2 b.i.d. for 14 days q21 days.

O-82. THE ANTI-TUMOUR EFFECTS OF CONJUGATED LINOLEIC ACID IN BREAST CANCER ARE MEDIATED BOTH BY P-53 DEPENDENT AND INDEPENDENT APOPTOTIC PATHWAYS

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Aims: The anti-tumour effects of the dietary fatty acid, conjugated linoleic acid (CLA), may be mediated through enhanced apoptosis. However, the effects of CLA on genes involved in apoptosis are unknown and this study examines the effects of

CLA on p53, p21WAF1 and bcl-2 expression in addition to the cytotoxic effects of CLA on breast tumour growth.

Methods: Oestrogen receptor positive and negative breast cancer cells (MCF7, MDA-MBA-231) were grown in supplemented RPMI media, containing CLA at concentrations (0 μM to 200 μM) for 24 hours. The effects on cell growth were assessed using MTT assay. Following treatment with CLA, northern blotting and ELISA were performed to determine the effects on the expression of p53, p21WAF1 and bcl-2.

Results: Exposure to CLA resulted in a dose dependent reduction in growth of MCF-7 cells - 20% at 6.25 μM, 50% at 100 μM and 65% at 200 μM ($p < 0.001$). Similar results were obtained for MDA-MBA-231 cells. Northern blot analysis showed that CLA treatment caused a dose dependent increase in wild-type p53 expression (MCF-7 cells) by 284% at 12.5 μM, 347% at 100 μM, and 523% at 200 μM of CLA ($p < 0.01$). There was no change in bcl-2 expression. The expression of p21WAF1, a key downstream regulator of p53, was raised to 203%. CLA did not change the expression of mutant p53 (present in MDA-MBA-231 cells) or p21WAF1, but did increase the expression of bcl-2 by 103% at 12.5 μM, 201% at 50 μM, and 207% at 100 μM of CLA ($p < 0.01$). Similar over-expression of the corresponding proteins were noted by ELISA.

Conclusions: This is the first demonstration which shows that CLA exerts its anti-tumour effects by increasing the expression of the wild-type p53 and the p21WAF1 gene. However, in cells with mutant p53, CLA inhibits cell growth, through a p53-independent pathway.

O-83. HYPERSENSITIVE K303R OESTROGEN RECEPTOR VARIANT NOT FOUND IN DUCTAL CARCINOMA *IN SITU*

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Non-atypical hyperplasia of the breast (hyperplasia of usual type) is believed to be a non-obligate precursor of breast cancer. As such, genetic abnormalities or mutations in such lesions may play a role in progression toward malignancy. One recently described mutation, occurring in about one third of hyperplasia tested is an A908G (K303R) change in the oestrogen receptor a gene that creates a hypersensitivity to oestradiol (Fuqua *et al.*, Cancer Res 2000, 60: 4026–4029).

We have examined a significant number of DCIS, by sequencing PCR products from microdissected samples.

No evidence of the A908G mutation was found, either individually or together with the wild-type allele. Enough cases of DCIS (44) were studied to make this results statistically significant ($P < 0.001$; Fisher Exact Test).

Retention of the A908G mutation in more advanced lesions, such as ductal carcinoma *in situ* (DCIS), would provide evidence that this mutation is involved in breast cancer progression. That the mutation was not found, leads us to believe that either the mutation is not retained during progression, that it may be involved only in the progression of lower grade DCIS, or that this mutation is limited to HUT that fail to progress via DCIS.

O-84. OESTROGEN WITHDRAWAL REDUCES EPITHELIAL CELL PROLIFERATION IN OESTROGEN RECEPTOR (ER) POSITIVE BUT NOT NEGATIVE DUCTAL CARCINOMA IN-SITU (DCIS)

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Aims: Over 50% of DCIS is ER negative which will not respond to hormone therapy. To investigate the effect of hormone manipulation on epithelial proliferation we studied 100 women who had undergone diagnostic core biopsy followed by surgery for DCIS 14–21 days later. ER status and ki67 (a measure of epithelial cell proliferation) was determined by counting 1,000 cells after immuno-histochemical staining on paired sections of the core biopsy and operative specimens for each woman. In ER negative DCIS epithelial proliferation did not change between diagnosis and treatment. Only in ER positive patients who stopped HRT was a fall in epithelial proliferation observed (see table).

Group	ER (No)	Median core Ki67 (IQR)	Operative Ki67 (IQR)	P value*
1. Never taken HRT	– (24)	9.8 (5.6–18.5)	11.3 (7.5–15.5)	0.92
(control)	+ (32)	8.2 (4.9–14.9)	7.7 (4.4–11.8)	0.49
2. Continued HRT	– (4)	11.4 (6.1–28.8)	16.0 (6.9–28.8)	1.00
	+(17)	8.8 (3.8–16.8)	8.8 (2.0–15.4)	0.76
3. Stopped HRT	– (6)	15.9 (10.5–24.4	16.4 (10.7–23.7)	0.94
	+ (15)	**9.3 (2.3–17.1)**	**3.3 (0.8–8.9)**	**0.04**

*Mann-Whitney 2-tailed test

Conclusions: Oestrogen withdrawal reduces proliferation in ER positive but not in ER negative DCIS. Therefore adjuvant anti-oestrogen therapy is likely only to benefit ER positive patients.

O-85. CHROMOSOMAL ALTERATIONS ASSOCIATED WITH TRANSFORMATION OF A TAMOXIFEN-SENSITIVE CELL LINE INTO ITS DRUG RESISTANT CLONE

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Introduction: Tamoxifen resistance is a serious problem in the management of breast cancer. Knowledge of the genetic pathways leading to tamoxifen resistance may allow the development of novel therapeutic strategies.

Aims: To determine the genetic changes between MCF-7 a tamoxifen sensitive human breast cancer cell line and its resistant clone CL-9 using comparative genomic hybridisation (CGH).