FEC100) ± H without unexpected toxicity. All pts with hormone receptor-positive tumours received adjuvant hormonal therapy.

Conclusions: These preliminary data confirm the safety of the proposed XT±H combination as neoadjuvant therapy for LABC, with promising pCR rates in the XT+H arm. Weekly XT is particularly attractive for treating HER2-positive tumours because it can be combined with H, the latter being cleared during the perioperative phase, thereby avoiding the risk of overlapping cardiac toxicity with anthracyclines. Additional data on recent pts will be presented at EBCC.

375 Poster

Switching from tamoxifen (TAM) to aromatase inhibitors (AIs) in the adjuvant treatment of breast cancer (BC) patients (pts). Results from the NORA study

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NORA study aimed at investigating modalities of treatment and pattern of relapse in 3511 BC pts, radically treated with surgery during the period 2000–2004, in 77 Oncological Centres.

Switching from TAM to AIs is one of the currently available options for the treatment of BC pts for whom hormone therapy is indicated. Recent trials are suggesting that switching to an AI during the period of the adjuvant therapy improves Disease-Free Survival (DFS) and Time to Distance reccurrence (TTDR). We analysed the switching from TAM to AIs in those patients who received either hormone therapy (HT) alone or chemotherapy (CHT) followed by HT as adjuvant treatment for early BC. 2388 out of 3511 (68%) started TAM, either as the sole therapy (35.3%) or after CHT. AIs have been administered as front-line choice in 392 pts (14.1%). Median age of pts receiving TAM was 58.6 (24–92). Switch was applied in 357 pts (17.2%). Median age of the switched pts was 62 (31–92). TN stage was T1N0 (34.6%), the therapy they have received was CHT followed by HT (59.7%). Median time to switch was 14.8 months (6.9–25.5). Main reasons for switching were gynecological toxicity (47%) and cardiovascular events (11.4%).

Switching from TAM to AIs was a current practice already some years ago, mainly due to TAM adverse events on gynecologic and vascular districts. Estimated DFS in the switched pts are currently under evaluation.

376 Poster

Preoperative dose-dense sequential chemotherapy of epirubicin/cyclophosphamide followed by docetaxel/capecitabine in patients with early breast cancer: preliminary results

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Aims: To evaluate the activity and safety of a dose-dense, sequential chemotherapy of epirubicin/cyclophosphamide (EC) followed by docetaxel/capecitabine (DXe) given preoperatively in patients with early breast cancer not candidate to breast-conserving surgery.

Patients and Methods: This was a Simon's two-step phase II study, recruiting 24 patients in the first step, and an additional 17 patients in the second step (total of 41 patients). Patients with untreated operable breast cancer (T2–3, N0–2, M0) received four cycles of EC (cyclophosphamide, 600 mg/m^2 and epirubicin, 90 mg/m^2) q2 weeks, followed by two cycles of DXe (docetaxel, 36 mg/m^2 days 1, 8, and 15 and capecitabine, 1250 mg/m^2 days 5–18) q 28 days, with pegfilgrastim support. The primary end point was the incidence of pathological complete response (pCR) in the breast. Secondary end points were clinical response, rate of breast conservation, and safety.

Results: Twenty-four out of 26 enrolled patients were evaluable for response to treatment (one patient withdrew from the study for G4 neutropenia after the first EC cycle, and the other for therapy refusal after the 4 EC cycles). A pCR was observed in 6 patients for a total pCR rate of 25%. This met the requirements of the study design for the first step. A clinical response (CR or PR) detected by palpation and by imaging was observed in 23 patients, for an overall response rate of 96%. The rate of breast-conserving surgery was 75%. The treatment was well tolerated: one patient experienced G3 mucositis and another patient required a 25% dose reduction of capecitabine because of hand-foot syndrome.

Conclusion: The dose-dense sequential combination EC/DXe is endowed with good antitumor activity and limited toxicity, allowing a high rate of pCR and breast conservation. Accrual is continuing up to the estimated sample size.

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377 Poster

The expression of Her-2, IGF-1R, IGF-1, ER alpha and ER beta in tamoxifen resistant breast cancers

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Introduction: Tamoxifen resistance poses a significant problem in treating certain oestrogen receptor(ER) positive breast cancers. Recent evidence suggests that over expression of HER-2 receptors and increased signaling in growth factor receptor pathways (EGFR-HER-2, IGF-1R) are responsible for this resistance. The role of ER-beta in Tamoxifen resistance remains controversial. This study examines the gene expression difference in Tamoxifen sensitive and resistant breast cancer.

Methodology: Tamoxifen-resistant breast cancer samples from 11 patients who failed to respond to neoadjuvant Tamoxifen (*Group A*) were obtained. Samples were also obtained from 11 patients who developed recurrence or metastasis at least 1 year after surgery and taking adjuvant Tamoxifen(*Group B*). Samples from 14 patients who had these criterias were employed as Tamoxifen-sensitive controls (*Group C*): considered high risk of developing further metastasis (grade 3 with lymph node metastasis); started on adjuvant Tamoxifen; did not develop evidence of recurrence or metastasis at 6-year follow-up. All samples were ER positive on immunostaining. Relative expressions of ER-alpha, ER-beta, HER-2, IGF-1 and IGF-1R in all these samples were measured using real-time quantitative PCR.

Results: Mean ER-alpha expression was slightly lower in Group A when compared to Group B and C. However, there was little difference in the other gene expressions in all the groups. In Group A, IGF-1R levels significantly increased with HER-2 levels ($P = 0.010$). IGF-1R increased marginally with ER-alpha in Group C ($P = 0.098$) and Group A ($P = 0.000$). In Group B and C, IGF-1 increased significantly with HER-2 and ER-alpha but not in the Group A samples. Only Group C showed a positive correlation between ER beta and IGF-1 ($P = 0.003$) samples. ER-beta increased with IGF-1R in all groups.

Conclusion: Mean ER-alpha was lower in tamoxifen resistant breast cancers. However a larger sample size in future studies is required to detect significant difference in gene expression in these groups. The relationship between (EGFR-)HER-2 and IGF-1R in Tamoxifen-resistance the samples suggests that cross-talk between the two growth factor pathways may contribute to tamoxifen resistance. The stimulatory effect of IGF-1 on ER alpha and ER beta expression may be lost in Tamoxifen-resistant cancers. The role of ER beta in tamoxifen resistance may lie in this relationship.

Thursday, 23 March 2006 16:00–16:45

POSTER SESSION

Locally advanced and recurrent disease

378 Poster

The effect on survival of local recurrence (LR) after breast conserving surgery

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This study is of 687 consecutive cases treated at Nottingham City Hospital in 1990–96 by breast conserving surgery (BCS). Cases were analysed by the Nottingham Prognostic Index (NPI).

Local recurrence (LR) is defined as recurrence within the parenchyma or skin of the treated breast; nodal recurrence is NOT included.

	n	LR		% survival		Death from breast cancer	
		no.	%	No LR	LR	Relative risk	p
EPG	144	21	15	99	81	19×	0.001
GPG	188	23	12	96	81	5×	0.089
MPG I	218	19	9	82	53	3×	0.003
MPG II	84	7	8	70	43	2×	0.085
PPG	42	9	21	65	7	2×	0.001
Total	676	79	12	87	63	3×	<0.001

LR rates (actuarial) are given to 108 months. Survival was analysed with/without LR.

Conclusions:

1. Cases which suffered prior LR had a worse survival (63% at 10 years) than those which did not (87%).
2. In all NPI groups survival was worse in those suffering LR.
3. The risk of death after LR in every prognostic group and the relative risk being higher in the best NPI groups, give strong evidence that it is the occurrence of LR rather than poor prognostic features coding for both death and LR.
4. The higher rates of LR in the EPG & GPG were brought about by the majority receiving neither RT nor Tamoxifen in these groups.

Local control is as important as the application of systemic therapies in improving survival.

379 Poster

Measurement of residual tumour size after neo-adjuvant chemotherapy for locally advanced breast cancer: accuracy of clinical examination, mammography, ultrasound and magnetic resonance imaging

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Introduction: In locally advanced breast cancer, neo-adjuvant chemotherapy is used to downsize the tumour and responders can undergo breast-conserving surgery instead of mastectomy. It is important therefore to have an accurate assessment of the residual disease after chemotherapy in order to plan the extent of surgery. Clinical assessment, mammogram and ultrasound are frequently used but the accuracy is not satisfactory. Magnetic resonance imaging (MRI) is increasing used to assess tumour extent in breast cancer. We examine the accuracy of residual tumour size measurement with these modalities by comparing with the pathological size after tumour resection.

Method: Patients with locally advanced breast cancer were prospectively recruited for neo-adjuvant chemotherapy. Chemotherapy consisted of an anthracycline-based regime. After chemotherapy, residual tumour was assessed by clinical examination, mammogram, ultrasound and MRI followed by definitive surgery.

Pathological size of residual tumour was correlated with the size measured by clinical examination, mammogram, ultrasound and MRI. Degree of correlation was measured by correlation analysis.

Result: Thirty-eight patients were recruited with a mean age of 43 (range 27 to 58). Mean tumour size was 69 mm (range from 37 to 130 mm). Eighteen patients (47%) had palpable axillary lymph node at presentation.

Clinical response was achieved in 30 patients (79%). Complete clinical response was seen in 7 patients (18%). Four patients (11%) had successful breast-conserving surgery and 29 underwent mastectomies. Two patients refuse operation after chemotherapy.

Clinical examination and MRI were significantly associated with pathological size (Pearson's correlation coefficient: 0.43 and 0.75 respectively). MRI gave better assessment than clinical examination. There was no significant correlation between pathological size and the size measured by mammogram or ultrasound.

Conclusion: Clinical examination and MRI gave significant correlation with residual tumour size. MRI was the best assessment of residual tumour size after neo-adjuvant chemotherapy.

380 Poster

Potential role of [18F]FDG-PET/CT in the evaluation of therapy response after neoadjuvant chemotherapy

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Background: [18F]FDG-PET/CT is usefull for staging of locally advanced breast cancer (LABC). In metastatic breast cancer, it is accurate in the evaluation of chemotherapy response. This study evaluates the accuracy of PET-CT in predicting residual invasive tumour in the breast and axillary lymph nodes following neoadjuvant chemotherapy.

Patients and Methods: Twenty women with non-metastatic LABC with [18F]FDG-PET/CT positive breast cancers and a clinical response on chemotherapy were evaluated post-chemotherapy for residual disease. Residual tumour as estimated from clinical breast examination (CBE) and breast imaging (ultrasound, mammography, MRI) was compared with [18F]FDG-PET/CT. Pathologic assessment provided the reference for pathologic tumor response.

Results: see the table.

	Breast pathology				Nodes pathology			
	CBE/Imaging		PET/CT		CBE/Imaging		PET/CT	
	Macro	Micro	Macro	Micro	Macro	Micro	Macro	Micro
Sensitivity	64.2%	60%	71.4%	66.7%	100%	46.2%	100%	46.2%
Specificity	83.3%	80%	100%	100%	86.7%	85.7%	93.3%	100%
+ pred. value	90%	90%	100%	100%	71.4%	85.7%	83.3%	100%
− pred. value	50%	40%	60%	50%	100%	46.2%	100%	50%

Conclusion: PET/CT is not of great help in the evaluation of efficacy of neoadjuvant chemotherapy. All 4 efficacy parameters are unsatisfactory to replace histopathology.

In 9/20 patients the result of the PET-CT did not match with residual disease in breast or axilla.

381 Poster

Breast cancer patients preferences for oral versus intravenous second-line anticancer therapy

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Background: several oral (PO) analogues of existing intravenous (IV) chemotherapeutic agents as well as more clinically efficient endocrine therapies (both oral and parenteral) are currently available to treat breast cancer patients with recurrent disease. Establishing patient perception regarding the route of anticancer therapy (ACT) may provide very useful information to help selecting from treatment alternatives that offer only small differences in survival, but might be less acceptable for patients. The study is aimed to elicit preferences for the route of eventual second-line ACT in women with early breast cancer.

Material and Methods: 528 consecutive cancer patients recruited in 3 centers fulfilled the following eligibility criteria to enter the study: 1) age between 20–75 years, 2) proper psychosomatic state to complete independently a therapy questionnaire preference, 3) at least 6 months interval between last course of chemotherapy and entering the study. The above group consisted of 263 breast cancer women (median age: 56, range: 27–75 years) without any evidence of disease, who completed their radical ACT 2–226 months (median: 36) before were interviewed. All the patients were directly asked about their preferences for the route of second-line ACT administration when the clinical efficacy and toxicity profiles are expected to be similar. Demographic and treatment-related data were collected by interviewers.

Results: 1) of 263 patients, 207 (78.7%) preferred PO ACT, 49 (18.6%) had not any preference (NP) and 7 (2.7%) wanted to be treated IV; 2) the most important reasons for this choice were convenience (limited ability to visit cancer center on regular basis), problems with IV access, and toxicity considerations (increased risk of IV-transmitted diseases) of the patients; 3) patients' choice was significantly associated with some clinical and