In patients with ER-negative disease (n = 304) goserelin was inferior to CMF for DFS (HR 1.61; 95% CI 1.20, 2.16) and the other two outcomes. With regard to overall safety, as reported previously, goserelin was well tolerated.
Conclusions: This follow-up analysis confirms the previously reported results from the ZEBRA trial and thus demonstrates that goserelin offers a well-tolerated effective alternative to CMF chemotherapy in the management of patients with ER-positive, node-positive early breast cancer.

O-4 Ovarian suppression (OS) and tamoxifen (TAM) as an alternative to chemotherapy in early breast cancer. Long-term results of the GROCTA02 trial

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Background: We have previously reported that comparable results can be achieved by 5 years of TAM combined with ovarian suppression or chemotherapy in pre-perimenopausal breast cancer patients affected by early breast cancer (JCO 18:2718–27, 2000). Here we report the updated results of this trial at a median follow-up time of 12 years.
Methods: Details have been published previously. In summary 124 women have been randomly assigned to receive TAM for 5 years in combination with some form of OS (most patients were given Goserelin injections for 2 yrs, but a few of them were restarded on Goserelin for one additional year when menses were restored) while 120 were given 6 cycles of "classical" (i.e. cyclophosphamide 100 mg/m^2 by mouth dd 1–14, every 4 weeks) CMF. In both groups, most of the patients were node positive (though about 15% of patients in each group were "high risk" node-negative) and all of them had ER positive tumours.
Results: At the time of the present analysis, in all 109 pts relapsed and 64 died. There was no statistically significant difference between groups either in progression-free or in overall survival (p = 0.7 for both comparisons). The comparability of results is confirmed by multivariate analysis (table below) which in addition shows that No of involved nodes and tumor grade are both independent predictors of recurrence and mortality risks.

	Recurrence			Death		
	HR	(95% CI)	P	HR	(95% CI)	P
Treatment						
CMF	1.0		0.8	1.0		0.8
TAM+OS	0.95	(0.64–1.40)		1.06	(0.64–1.77)	
Age						
⩽40 years	1.0		0.015	1.0	0.2	
>40 years	0.56	(0.35–0.89)		0.66	(0.36–1.21)	
Tumour size						
⩽2 cm	1.0		0.2	1.0		0.03
>2 cm	1.26	(0.85–1.86)		1.78	(1.05–3.01)	
No. of involved nodes						
0–3	1.0		0.002	1.0		0.055
>3	1.89	(1.27–2.84)		1.67	(0.99–2.81)	
Tumour grade						
G1–G2–Gx	1.0		0.02	1.0		0.015
G3–Gu	1.67	(1.07–2.59)		1.99	(1.15–3.44)	

Outcome analysis by prognostic strata confirms that comparable results were achieved by TAM plus OS or CMF, except in patients affected by undifferentiated tumors where both recurrence-free and mortality trends favoured those assigned to CMF (the difference in respect to mortality risk being statistically significant: p = 0.02)

Conclusions: The updated results of GROCTA 2 trial confirm that, even after a long follow-up, OS and TAM is an effective alternative treatment for ER positive breast cancer patients, irrespective of nodal status, though CT appears to be more appropriate to manage the women with less differentiated tumours.

O-5 Carcinoembryonic antigen cell adhesion molecule (CEACAM6) predicts breast cancer recurrence following adjuvant tamoxifen

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Tamoxifen has been the principal endocrine therapy for ERα-positive breast cancer patients and still remains the therapy of choice in the pre-menopausal setting. However, resistance and recurrence remain a serious problem. Our previous work has indicated that CEACAM6 was significantly up-regulated in tamoxifen-resistant (TAMr) MCF-7 derivatives compared to sensitive controls. The aim of this study was to determine the functional role of CEACAM6 in endocrine resistant breast cancer and to retrospectively test whether it was predictive of resistance in a large cohort of breast cancers with long term follow up. Up-regulation of CEACAM6 mRNA and protein in TAMr MCF-7 was confirmed by qRT-PCR and Western blotting. SiRNA-mediated silencing of CEACAM6 reduced clonogenicity of TAMr cells by ~3-fold ($p < 0.05$), and reduced anchorage-independent colony formation by ~10-fold ($p < 0.05$). Importantly, silencing of CEACAM6 partially restored sensitivity of TAMr cells to 4-Hydroxytamoxifen and restored their ability to proliferate in response to 17β-estradiol. CEACAM6 immunohistochemistry was performed on a tissue microarray comprising 108 relapsed primary human breast cancers and 243 tamoxifen-sensitive controls. Cytoplasmic and membranous staining was scored, with a maximum score of 3 indicating strong staining in >10% of cells. 57/108 (53%) of the relapsed group demonstrated strong to moderate CEACAM6 staining, which was significantly more than the non-relapsed group (76/243 (31.3%) OR = 2.46, 95% CI 1.54 to 3.91, $p < 0.0001$). In conclusion, our *in vitro* and clinical data support an important role for CEACAM6 in endocrine resistance and breast cancer recurrence.

O-6 Three years of the Breast Cancer Clinical Outcome Measures (BCCOM) project

I. Monypenny*, C. Lagord, O. Kearins, G. Lawrence, on behalf of the BCCOM Steering Group. *The BCCOM Project, supported by Breakthrough Breast Cancer, aims to set up routine methods to collect data on symptomatic breast cancers in males and females diagnosed and treated in the UK and to use the data to develop outcome measures to monitor performance.*

Data on over 45,700 primary symptomatic breast cancers diagnosed in 2002, 2003 and 2004 have been collected in the first three years of the project, including data on 374 male breast cancers. Each year, an average of 20,000 cases was sent to more than 200 UK consultant surgeons for checking.
In the absence of robust performance indicators, a set of measures has been developed by the BCCOM Project Steering Group. For example "the number and proportion of histologically node negative cancers for which more than seven nodes were harvested". BCCOM data indicate that 62% of invasive cases had known nodal status and that 52% were node negative. 59% (7,983 cases) of the node negative cancers had more than 7 nodes harvested. 46% of

these cases underwent a mastectomy; whereas the overall mastectomy rate was 50%.
Analysis of the cases collated by the BCCOM project in years 1–3 will be undertaken to evaluate data quality and performance. Delegates at the conference will be invited to comment on the measures developed, and the use of these measures as possible surrogates for patients' clinical outcomes will be discussed.

O-7 Micro-RNA expression profiling in primary breast tumours

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Introduction: The role of micro-RNAs in the regulation of proliferation, differentiation and apopotosis has advocated them as a novel molecular mechanism in the aetiology of carcinogenesis. MicroRNA expression has been shown to be dysregulated in a number of human cancers, including breast cancer.
Aims: To identify microRNAs that are abberantly expressed in breast tumour tissue and examine correlations with established clinicopathological variables.
Methods: Whole genome microRNA profiling was performed in six early stage breast cancer specimens. Expression of selected differentially expressed microRNAs was validated using RQ-PCR in a larger cohort of 54 breast tumours, 5 benign, and 5 normal breast tissues. Associations between relative expression of specific microRNAs, established clinicopathological variables and hormone receptor status were examined.
Results: 53 of 452 microRNAs were differentially expressed across the six tumour samples. Specific microRNAs which were validated in the larger cohort of samples using RT-Q-PCR included *miR-21, miR-195, miR-10b* and *miR-154**. Tumour samples exhibited higher *miR-21* expression than normal breast tissue. Conversely, *miR-10b* and *miR-195* were consistently expressed at lower levels in tumour versus benign and normal breast tissue. *MiR-195* and *miR-154** expression was significantly lower in oestrogen receptor positive *(ER)* than *ER* negative tumours. ($p = 0.005$, $p = 0.001$). Expression was independent of other cliniopathological variables.
Conclusions: The increased expression of *miR21* and decreased expression of *miR-10b* and *miR-195* in tumor tissues implicates these miRNAs in oncogenesis and tumour suppression respectively. We have shown that *miR-195* and *miR-154** are differentially expressed in breast tumours according to *ER* status, highlighting their importance in specific breast cancer phenotypes.

O-8 Factors predicting survival after neoadjuvant therapy with aromatase inhibitors

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Background: Few studies have investigated factors predicting outcome following neoadjuvant endocrine therapy. This study aimed to determine factors predicting survival after neoadjuvant treatment with aromatase inhibitors (AI's).
Methods: 153 postmenopausal women with large/locally advanced estrogen receptor rich tumours (ER 5–8) were treated for 3 months with letrozole, anastrozole or, exemestane. The mean patient age was 74.7 years. Tumour biopsies were obtained prior to starting therapy and at 3 months. At 3 months patients underwent surgery with nodal assessment or, continued AI therapy. Responding patients continued AI therapy post-operatively. Median follow up was 41 months. Five year survival was 63.1% and cause specific survival (CSS) 79.8%.
Results: At 3 months only 3% had progressive disease and 67 had responded (>50% reduction in volume). In the univariate analysis T stage ($p = 0.03$), surgical node status ($p = 0.0005$), Ki67 at diagnosis ($p = 0.036$), 3 month % reduction in Ki67 ($p = 0.0027$) and 3 month Ki67 ($p = 0.03$) were significantly correlated with CSS. In the proportional hazards analysis significant variables were number of positive nodes ($p = 0.0007$), % reduction in Ki67 ($p = 0.0029$) and, tumour grade ($p = 0.0383$). Excluding those available at diagnosis significant variables were baseline Ki67 ($p = 0.02$) and T stage ($p = 0.02$).
Conclusion: In post-menopausal women treated with neoadjuvant AI therapy: (i) Two thirds with ER rich large/locally advanced breast cancers responded to 3 months of treatment and, (ii) Surgical node status, % reduction in Ki67 and, tumour grade predicted death from breast cancer.

O-9 ONCOPOOL – A European Database in 16,893 cases of breast cancer: comparison with SEER

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11 European Breast Units from 10 countries retrospectively entered consecutive cases diagnosed in each unit in periods between 1990–99. Cases were women, age $\leqslant 70$ with primary tumours <5 cm diameter. Data on diagnosis, surgical and adjuvant treatments, pathology and biology, recurrences and survival.

- Factors at diagnosis
  - Tumour size: 21% $\leqslant$1 cm, 28% $\leqslant$2, 29% $\leqslant$3, 10% $\leqslant$4.9
  - LN status: LN neg 66%, LN 1–3+ 24%, LN 3+ 10%
  - Grade: I 29%, II 42%, III 29%
- Second order polynomial curves demonstrate the relations of the three LN stages with tumour size and between grade and stage
- Overall survival was 91% 5 yr, 81% 10 yr and 78% 14 yr (Life table)
- The survival data provides validation of the updated prognosis according to the Nottingham Prognostic Index (to be separately presented).

The US SEER (Surveillance, Epidemiology and End Results) Database has long been regarded as giving the standards in Primary Breast Cancer for distribution of pathological factors and prognoses. There was a great amount of incomplete data.
Comparison of the SEER estimates of prognosis according to TNM are shown in ONCOPOOL to be greatly inferior to other means of estimation (Table).

	TNM	NPI Predicted			ONCOPOOL
	Predicted 10 yr % OS	Grade	NPI Group	10 yr % BCS	Observed 10 yr % BCS
$\leqslant$2 cm, LN –	94	I	EPG	96	94
$\leqslant$2 cm, LN –	94	III	MPG I	81	94
$\leqslant$2.5 cm, LN –	88	I	GPG I	93	93
$\leqslant$2.5 cm, LN –	88	III	MPG II	74	76
$\leqslant$2.5 cm, LN –	76	I	MPG I	81	84
$\leqslant$2 cm, LN –	76	III	PPG	55	53
$\leqslant$2 cm, LN –	58	I	MPG II	74	76
$\leqslant$2.5 cm, LN –	58	III	PPG	55	53