adjuvant systemic therapy have been withdrawn from this analysis.
Analyses: Breast cancer specific survival (BCS) by life table.
Results: Median follow-up 8.8 years (2.5–13.9). 2,499 cases were ⩽ did not receive adjuvant therapy.
Table I, of these 2499 cases 1051 were <10 mm

Diam		n	BCS survival 10 yr %
<10 mm	All	1051	94±1
<10 mm	LN neg, gr I	569	97±1
<10 mm	LN neg, gr III	142	83±3

To base selection of cancers with over 90% survival without adjuvant therapy on ⩽10 mm, LN neg, is insufficient; grade must be considered.
Table II, 2499 <20 mm analysed by the Nottingham Prognostic Index (NPI) NPI = Grade (I-III) + LN status (Neg, + 1–3, + >4) +size (cm ×0.2)

NPI	NPI Group	n	BCS Survival 10 yr %
	All <20 mm	2499	86±1
<2.4	Excellent (EPG)	1117	96±1
2.41–3.4	Good (GPG)	886	92±1
3.41+	Other Groups	496	All <90%

The addition of LVI to NPI made no significant difference to the results.
Conclusion: The highest sensitivity and specificity for selection of tumours with BCS over 90% at 10 years is by NPI, selecting 80% of all tumours ⩽20 mm (n = 2,003) and additionally recognising 264 >20 mm. This compares with ⩽10 mm, LN neg, grade I selecting only 1,051 cases.

O-47 Gene expression profile associated with docetaxel resistance in breast cancer cells

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The mechanisms of resistance to docetaxel are poorly understood. The purpose of this study was to investigate the genetic pathways involved in docetaxel resistance using a unique model of docetaxel resistance, which we have developed in breast cancer cells.
We made two breast cancer cell lines, MCF-7 and MDA-MB-231, resistant by exposure to increasing docetaxel concentrations. The resultant sublines were able to withstand 1, 10 and 30 μM of docetaxel. Alterations of gene expression were determined using Affymetrix Genechip cDNA microarrays, and subsequently validated by RT-PCR and western analysis.
After selecting out gene changes that were common between both sets of sensitive cell lines and their resistant sublines (>2 fold), further normalisation and statistical filtering (ANOVA, assuming unequal variances, and the Benjamin-Hobbson false discovery rate applied as a multiple correction factor with a significance level of $p < 0.01$), we identified a 14 probe-set, encoding 10 genes (including p-glycoprotein), which were significantly associated with resistance to docetaxel. This probe set was interrogated for predictive value using Support Vector Machine algorithm (using Fisher's Exact test and Gaussian kernal function) and Principal Component Analysis on Conditions was applied to identify similar groups of gene expression between all the cell lines.
These changes, therefore, may represent common mechanisms of resistance in breast cancer cells, and may be able to predict response. In addition, this is the first description, using microarray analysis, to identify the genetic pathways involved in the evolution of acquired resistance to docetaxel in a cell line model.

O-48 Tolerability of zoledronic acid – first safety data from the AZURE Trial (BIG01/04)

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The AZURE trial was designed to determine whether Zoledronic acid (Z) improves the disease-free and bone metastasis-free survival of women with stage II/III breast cancer. 3207 eligible patients received (neo)adjuvant chemotherapy (CT) and were randomised to no additional treatment or Z 4 mg iv every 3–4 weeks during CT, then every 3–6 months to 5 years. To correspond with timing of CT, serious (SAE) and non-serious adverse event (AE) data within 6 months of randomisation were compared.
939 SAE and 33859 AE have been reported to date. No significant differences in the numbers of patients with any SAE (324 [20%] CT, 373 [23%] CT+Z), or neutropaenic sepsis SAE (157 CT v 155 CT+Z respectively) were seen. CTC grade 3/4 AE occurred in 4.6% and 4.8% with CT and CT+Z respectively. The frequency of CT dose reductions (17% CT, 14% CT+Z) and median duration of CT (3.52 months CT, 3.48 months CT+Z) were similar, confirming that Z has no significant effect on CT delivery. 9 cases of osteonecrosis of the jaw have been confirmed to date (all reported cases).
This is the largest safety analysis of Z in patients without the confounding influence of metastatic disease and indicates that Z can be safely combined with adjuvant chemotherapy.

O-49 A phase III trial of Gemcitabine plus Docetaxel (GD) versus Capecitabine plus Docetaxel (CD) for patients (pt) with anthracycline-pretreated metastatic breast cancer

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Background: Patients (Pts) with anthracyclines pre-treated MBC frequently receive combination chemotherapy with a taxane and an antimetabolite such as gemcitabine or capecitabine. This trial compared the-(GD) combination with the (CD) combination, in this clinical setting. The primary objective of the trial was a comparison of the progression-free survival (PFS) difference between the two treatment groups, and the secondary objectives included overall response rate (ORR), time to treatment failure (TtTF), overall survival (OS), and toxicity assessments. In a previous analysis GD demonstrated similar efficacy to CD but with a better non-hematological toxicity profile [Chan et al, ASCO 2005]. This reports the final analysis of the results including OS.
Methodology: Pts with histologically/cytologically confirmed MBC, who had received an anthracycline-based regimen in the neoadjuvant/adjuvant/or first-line metastatic setting, were randomized to GD ($G = 1000\ mg/m^2$ d1, 8; $D = 75\ mg/m^2$ d1) or CD ($C = 2500\ mg/m^2$ daily d1 to 14; $D = 75\ mg/m^2$ d1) q21 days.
Results: Characteristics of the 305 included patients (GD = 153; CD = 152) were previously reported. A median of 6 cycles was delivered on both arms. CTC grade 3/4 hematologic toxicity was similar in both arms, except for grade 3/4 thrombocytopenia GD = 11%; CD = 3%; $p = 0.014$). The fact that blood test was performed at day 8 in the GD (pts received iv chemotherapy) but not the CD arm of the trial, may explain this difference. Nonhematologic toxicities were low in both arms, but