which could be used to tailor treatment to individual patients. Most chemotherapeutic agents preferentially target proliferating and cycling cells, which results in mitotic catastrophe and apoptosis. We therefore hypothesized that the level of Bcl2 protein, which is a cell cycle/apoptosis regulator, could predict response and clinical outcome to these agents.
**Material and Methods:** Bcl2 expression was immunohistochemically evaluated in high risk (Nottingham prognostic index >3.4) luminal "ER+/HER2−" breast cancer from four independent series; (a) 135 BC patients treated with surgery + radiotherapy at Nottingham City hospital before 1986 who did not receive any endocrine therapy, (b) 430 BC patients treated with surgery + radiotherapy followed by Tamoxifen therapies, (c) 179 BC patients treated with surgery + radiotherapy followed by Tamoxifen and anthracycline-based chemotherapy and (d) 70 locally advanced primary BC patients treated with an anthracycline-based combination (FEC) followed by surgery + radiotherapy and Tamoxifen.
**Results:** Luminal BC patients with low Bcl2 expression had 2 to 4 fold increase risk of death and recurrence compared to those with high Bcl2 irrespective of Tamoxifen treatment (Table 1). After anthracycline-based neo-adjuvant chemotherapy, 33% of low Bcl2 expression luminal BC achieved pCR vs. 7% of high Bcl2 expression luminal BC (p = 0.02). Luminal BC patients with low or high Bcl2 expression who had received anthracycline based combined therapy in addition to Tamoxifen in either neo-adjuvant or adjuvant sittings had similar BC specific survival and progression free survival (p = NS).

Table 1

| Variable | Breast cancer specific survival | | Progression free survival | |
|---|---|---|---|---|
| | HR (95% CI) | P | HR (95% CI) | P |
| High risk luminal breast cancer patients who did not received Tamoxifen (n = 135) | | | | |
| Bcl2+ | 1 | 0.00006 | 1 | 0.003 |
| Bcl2− | 3.7 (1.9−6.9) | | 2.3 (1.3−4.0) | |
| High risk luminal breast cancer patients who received Tamoxifen (n = 430) | | | | |
| Bcl2+ | 1 | 0.00000001 | 1 | 0.0000003 |
| Bcl2− | 2.6 (1.8−3.7) | | 2.1 (1.5−2.9) | |

**Conclusions:** Low Bcl2 expression was associated with poor prognosis of high risk luminal BC irrespective of hormone therapy. Bcl2 status could predict the potential benefit of anthracycline based chemotherapy of luminal BC which is resistance to Tamoxifen. Clinical trials based on Bcl2 expression in luminal breast cancer are warranted.

**5176** POSTER

**Gene Expression Profiles Predict Pathological Complete Response to Standard Neoadjuvant Fluorouracil, Doxorubicin, and Cyclophosphamide and Paclitaxel With or Without Trastuzumab in Early Breast Cancer**

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**Background:** To examine the feasibility of gene expression signature as a predictor of pathological complete response (pCR) to sequential fluorouracil, doxorubicin, and cyclophosphamide (FEC) and weekly paclitaxel (P) with or without trastuzumab (T) neoadjuvant chemotherapy.
**Materials and Methods:** We have conducted consecutive two prospective phase II, establishing training and validation sets, with similar eligible criteria include, stage IIA-IIIC, chemotherapy-naïve, measurable disease, age ⩾20, PS 0/1, and adequate organ function. Patients were treated preoperatively with 4 cycles of FEC (500/100/500 mg/m$^2$) followed by 12 cycles of weekly P (80 mg/m$^2$) with or without T (2 mg/kg). Patients underwent pretreatment fine-needle biopsy for cDNA microarray using Affimetrix Gene Chip U133 plus 2.0 arrays with 30,000 differential expressions of various genes. We ranked gene probes from training sets according to a predictive power concerning pCR by Wilcoxon, and validated them using validation sets by SVM.
**Results:** Between July 2007 and December 2010, 122 patients were enrolled in the two consecutive prospective studies (training: 89 pts, validation: 33 pts). Median age was 51. PS 0/1: 115/7; Stage IIA/IIB/IIIA/IIIB/IIIC: 30/57/20/14/1; Histological subtype: ER+HER2- (LA)/ER+HER2+ (LB)/ER-HER2- (TN)/ER-HER2+ (enrich-HER): 51/18/24/29. All patients have received curable operations. pCR rate was 31.1% (LA; 2.0%, LB; 44.4%, TN; 37.5%, enrich-HER; 69.0%). 104 (85.2%) sufficient mRNA for cDNA microarray from individual primary breast cancer tissues fine-needle biopsy are available. As reported previously, the breast cancers were classified into a Luminal A/B, Basal-like, HER2-enriched, Claudin-low intrinsic subtypes, indicating a high quality of the representative method. In HER2 positive breast cancer, HER2-enriched subtype was a reproductive predictive marker. In contrast, In HER2 negative breast cancer, three genes (N-myc and STAT interacter, Tryptophanyl-tRNA synthetase, and IQCE) and basal-like subtype were validated as the predictors of pCR. The three genes were also identified as predictors of pCR in the triple negative population.
**Conclusions:** Specific gene expression profiles predict pCR to standard neoadjuvant regimen, especially in triple negative breast cancer.

**5177** POSTER

**Correlation Between PARP-1 Expression and In-vitro Chemotherapy Sensitivity in Patients With Breast Cancer**

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**Background:** Expression of Poly-A-Ribose-Polymerase-1 (PARP-1) has come into scientific focus based on its potential exploitation as a therapeutic target through PARP inhibitors. Furthermore, it could recently be demonstrated that cytoplasmic expression of PARP-1 varies depending on molecular breast cancer subtypes and is correlated with an increased response to neoadjuvant taxane-anthrazykline containing chemotherapy (von Minckwitz et al., J Clin Oncol (in press)). *In-vitro*-chemotherapy sensitivity and resistance assays (CSRAs) allow for the direct measurement of chemotherapy sensitivity in a given tumour independent of host factors.
**Methods:** We conducted an immunohistochemical tissue-microarray (TMA) analysis of 550 samples of invasive breast cancers with regard to expression of a set of molecular markers including estrogen receptor (ER), progesterone receptor (PR) and HER2 as well as PARP-1. Triple negative breast cancers (TNBC) were identified through lack of expression of ER, PR and HER2. All cancers were analyzed in an *in vitro* CSRA analysis for epirubicin/docetaxel (ED) and epirubicin/cyclophosphamide (EC). *In-vitro*-chemotherapy sensitivity was analyzed using an adenosine triphosphate (ATP) bioluminescence assay.
**Results:** A moderate/high PARP-1 expression was found in 48 and 33% of cases with TNBC and non-TNBC, respectively (p = 0.015). A correlation between TNBC phenotype and cytoplasmic expression was not observed. Instead, an increased both cytoplasmic and nuclear expression of PARP-1 was correlated with an increased *in-vitro* sensitivity against ED (p = 0.012 and 0.025, respectively) but not EC (p = 0.27 and 0.62, respectively).
**Conclusion:** Our results support previous observations in that expression of PARP-1 is correlated with an increased sensitivity against taxane-anthracycline chemotherapy independent of tumour phenotype.

**5178** POSTER

**Response of Immunohistochemically (IHC) Defined Breast Cancer Sub-types to Dose-dense Sequential Adjuvant Chemotherapy. Pooled Analysis of Two Randomized Hellenic Cooperative Oncology Group (HeCOG) Phase III Trials**

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**Background:** To investigate the efficacy of adjuvant dose-dense sequential chemotherapy with epirubicin, paclitaxel and CMF in sub-groups of patients with high-risk operable breast cancer, according to immunohistochemically (IHC) defined tumour sub-types.
**Materials and Methods:** Formalin-fixed paraffin-embedded (FFPE) tumour tissue blocks from 1030 patients (72% of the eligible patients) participating in two adjuvant dose-dense sequential chemotherapy phase III trials (HE 10/97 and HE 10/00) were centrally assessed in TMAs by IHC for 6 biological markers, i.e. estrogen receptor (ER), progesterone receptor (PgR), human epidermal growth factor receptor 2 (HER2), Ki67, cytokeratin 5 (CK5), and epidermal growth factor receptor 1 (EGFR). Cases with HER2 IHC 2+ were further evaluated by CISH or FISH. Patients were classified as Luminal A (ER-positive and/or PgR-positive, HER2-negative); Luminal B (ER-positive and/or PgR-positive, Ki67⩾14); Luminal-HER2 (ER-positive