manual method, 5.2% and 8.1%; 2D automated, 7.6 % and 8.1%; and 3D automated, 8.2% and 8.8%, respectively.

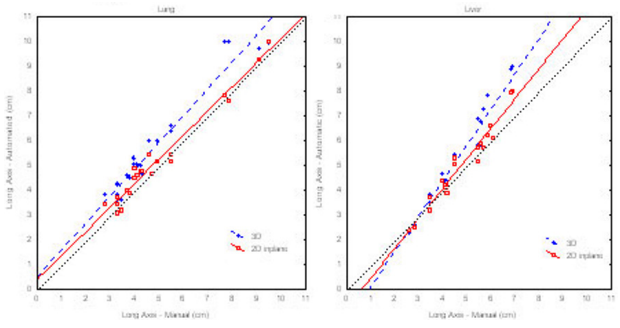

Fig. 1. Correlation of automated 2D *vs*. manual inplane long-axis measurements for lung (left) and liver (right) tumors (black dotted line represents perfect correlation).

Conclusions: Scan-rescan measurements of tumor size can be made with reproducibility in the range 5–9%, with no significant differences between manual and automated methods. There were no significant differences in assessments of size between inplane manual and 2D automated methods, but 3D derived measurements were significantly larger, which, for liver lesions, showed divergence from manual and automated inplane 2D.

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Effect of population and gender on chemotherapeutic agent-induced cytotoxicity

R.S. Huang[1], E.O. Kistner[2], W.K. Bleibel[1], S.J. Shukla[3], M.E. Dolan[1].
[1]University of Chicago, Department of Medicine, Chicago, IL, USA;
[2]University of Chicago, Department of Health Studies, Chicago, IL, USA;
[3]University of Chicago, Department of Human Genetics, Chicago, IL, USA

Large inter-individual variance is observed in both response and toxicity associated with chemotherapy. Our goal is to identify factors that contribute to chemotherapy-induced toxicity. To this end, we used EBV-transformed B-lymphoblastoid HapMap cell lines derived from thirty Yoruban trios (African descent) and thirty CEPH trios (European descent) to evaluate population and gender specific differences regarding cytotoxicity of carboplatin, cisplatin, daunorubicin and etoposide using a high throughput, short-term alamarBlue™ assay. The IC_{50} was compared for population and gender specific differences for the four drugs. We observed large inter-individual variance in IC_{50} values for carboplatin, cisplatin, daunorubicin and etoposide for both Yoruban and CEPH populations (range from 8- to 433-fold). Statistically significant differences in carboplatin and daunorubicin IC_{50} were demonstrated when comparing Yoruban cell lines ($n = 89$) to CEPH cell lines ($n = 87$) ($p = 0.002$ and $p = 0.029$, respectively). This population difference in treatment induced cytotoxicity was not seen for either cisplatin or etoposide. In the Yoruban population, cell lines derived from females were less sensitive to platinating agents than males [median carboplatin IC_{50} 29.1 vs 24.6 M ($p = 0.012$); median cisplatin IC_{50} 7.0 vs 6.0 M ($p = 0.020$) in female and male, respectively]. This difference was not observed in the CEPH population. These results demonstrate that population and gender may affect risk for toxicities associated with certain chemotherapeutic agents.

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The role of the novel apoptosis related gene BCL2L12 in prognosis and individualized treatment of breast cancer: a molecular and clinical approach

H. Thomadaki[1], M. Talieri[2], A. Ardavanis[3], A. Scorilas[4]. *[1]National and Kapodistrian University of Athens, Faculty of Biology, Biochemistry and Molecular Biology, Athens, Greece; [2]"Saint Savvas" Hospital, "G. Papanicolaou" Research Center of Oncology, Athens, Greece; [3]St. Savvas Anticancer-Oncologic Hospital, 31st Department of Medical Oncology, Athens, Greece; [4]National and Kapodistrian University of Athens, Faculty of Biology, Biochemistry and Molecular Biology, Athens, Greece*

Background: Breast cancer is a major health problem. The currently most successful approach for combating breast cancer is by early diagnosis, good prognosis and administration of effective treatment. A multitude of markers have been discovered within the last three decades, including factors related to different cell functions, such as apoptosis, with many members of the *BCL2* family of apoptosis-related genes being found to be differentially expressed in various malignancies, and some regulating cellular fate after exposure to anticancer drugs. A new member of the *BCL2* gene family, *BCL2L12*, was discovered and cloned (Scorilas et al. 2001) and it was found to be expressed in mammary gland. It maps to chromosome 19q13.3 and is localized between the *IRF3* and *RRAS* oncogene. Our objective is to investigate the novel gene *BCL2L12*, as a novel molecular biomarker for prognosis and individualized treatment of breast cancer.
Materials and Methods: In the present study, we explored the research on the prognostic value of *BCL2L12*, as a novel breast cancer biomarker. Sixty specimens from patients with, histologically confirmed, epithelial breast carcinoma were analyzed for *BCL2L12* gene expression by RT-PCR using gene specific primers. Actin was used as a control gene. Their gene expression profile was associated with clinicopathological parameters and survival analysis regarding to relapse and death were evaluated by constructing Kaplain-Meier curves and developing a Cox proportional hazard regression model.
We also studied the possible alterations in the mRNA expression of the apoptosis-related gene *BCL2L12* after cell treatment with cisplatin or carboplatin, in the breast cancer cell lines MCF7 and BT-20. The cytotoxic effect of each drug was evaluated by the MTT method and trypan blue staining, whereas the expression levels of distinct apoptosis-related genes were analysed by RT-PCR, using gene specific primers.
Results: Increased expression of *BCL2L12* gene was found in estrogen receptors positive as well as in chemotherapy responded patients. In addition, *BCL2L12*-positive patients were found to be almost 4 times less likely to relapse or die in comparison to *BCL2L12*-negative patients. Furthermore, treatment of the breast cancer cell lines, MCF-7 and BT20, with well-known chemotherapeutic drugs induces distinct alterations in the mRNA expression levels of *BCL2L12* gene, giving some preliminary information about its value in chemotherapy response prediction.
Conclusions: *BCL2L12* is involved in both breast cancer progression and in chemotherapy response, implying a possible role in individualized medicine and its application into more successful therapeutic interventions.
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Comparison of cell death ELISAs applied as potential surrogate biomarkers in the clinical evaluation of AEG35156 (XIAP antisense)

J. Cummings[1], T.H. Ward[1], M. Ranson[2], N.K. Smith[1], D. Jodrell[3], L. Robson[4], E. Dean[1], C. Dive[1]. *[1]Paterson Institute for Cancer Reserach, Clinical and Experimental Pharmacology, Manchester, United Kingdom; [2]Christie Hospital NHS Trust, Department of Medical Oncology, Manchester, United Kingdom; [3]Western General Hospital, Cancer Research Centre, Edinburgh, United Kingdom; [4]Cancer Research UK, Drug Development Office, London, United Kingdom*

The protein XIAP is the most potent endogenous inhibitor of caspase function currently known, and its over-expression is associated with poor patient outcome. AEG35156 is a second generation 19-mer oligonucleotide targeting XIAP and is currently undergoing early clinical trials. One of the anticipated outcomes of AEG35156 treatment is the induction of tumour cell death. We have studied 3 different plasma ELISAs as pharmacodynamic biomarkers during a CRUK Phase I trial of AEG35156 administered as a 7 day infusion. M30 Apoptosense detects a caspase cleaved fragment of the epithelial cell protein cytokeratin 18 (CK18) as a selective marker of apoptosis. M65 detects both intact and caspase cleaved CK18 as markers of apoptotic and non-apoptotic cell death. Quantitation of circulating nucleosomal DNA (nDNA) offers a further approach to apoptosis measurement. The 3 assays were utilised to analyse plasma samples collected at multiple time points spanning the first three week treatment cycle from 20 patients who had received AEG35156 at multiple dose levels from 48 to160 mg/m^2/d, where dose limiting transaminitis was encountered. Baseline concentrations of M30 and M65 antigens exhibited a 15 fold range. Similar values to those of healthy subjects were seen in patients with non-epithelial tumours (60–300 U/L). Very high values of 1600–3200 U/L were recorded in 2 patients with breast cancer. Analysis of two independent pre-treatment samples showed only minor variations in M30 and M65 antigens (<15%), whereas greater variability was detected with the nDNA assay. Increases in M30, M65 and nDNA antigens occurred with greater frequency at the higher doses of AEG35156, normally reaching a peak during the 7-day drug infusion. Increases in M30 and M65 antigens were also detected in patients with non-epithelial tumours, suggesting that these assays may also detect toxicity in non-tumour tissues. In 50% of patients, the concentration-time profiles for all 3 assays showed close temporal agreement. In a further subset of patients good temporal agreement was observed between nDNA and M65. In conclusion, the 3 ELISA assays appear to detect drug induced changes in circulating levels of their