# Four best poster abstracts - Oral presentations

**OP62**

**Polymorphisms in AKT1 and EGFR as possible new biomarkers of clinical outcome and toxicity in non-small-cell lung cancer patients treated with gefitinib**

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**Background:** EGFR mutations are strongly predictive of EGFR-TKIs activity in non-small-cell lung cancer (NSCLC), but resistance mechanisms are not completely understood. The interindividual variability in toxicity also points out to the need of novel pharmacogenetic markers to select patients before therapy. Therefore, we evaluated associations between EGFR and AKT1 polymorphisms and outcome/toxicity in gefitinib-treated NSCLC patients.
**Materials and Methods:** EGFR −191C/A and R497K, and AKT1-SNP3 and SNP4 polymorphisms and EGFR and K-Ras mutations were assessed in DNA isolated from blood samples and/or paraffin-embedded tumor from 96 gefitinib-treated NSCLC patients. Univariate and multivariate analyses compared genetic variants with clinical efficacy and toxicity using Fisher's, log-rank test and Cox's proportional hazards model. AKT1-SNP4 association with survival was also evaluated in 127 chemotherapy-treated/gefitinib-naive NSCLC patients, while its relationship with AKT1 expression and gefitinib cytotoxicity was studied in 15 NSCLC cell lines.
**Results:** AKT1-SNP4 A/A genotype was associated with shorter time-to-progression (TTP, $P = 0.04$) and survival (OS, $P = 0.01$). Multivariate analyses and comparison with the gefitinib-untreated population underlined its predictive significance, while the in vitro studies showed its association with lower AKT1 mRNA levels and gefitinib resistance. In contrast, EGFR activating mutations were significantly correlated with response, and longer TTP and OS, while both the EGFR −191C/A ($P < 0.001$) and the EGFR R497K ($P = 0.01$) polymorphisms were strongly associated with grade >1 diarrhea.
**Conclusion:** AKT1-SNP4 A/A genotype appears to be a candidate biomarker of primary resistance, while EGFR −191 and R497K polymorphisms are associated with diarrhea when using gefitinib in NSCLC patients, thus offering potential new tools for treatment optimization.

**OP82**

**Diagnostic performance of soluble mesothelin and megakaryocyte potentiating factor as biomarkers of mesothelioma**

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**Background:** Soluble mesothelin (SM) is currently considered the reference serum biomarker of malignant pleural mesothelioma (MPM). Megakaryocyte potentiating factor (MPF), the soluble fraction of the mesothelin precursor protein, has theoretical advantages over SM, suggesting a superior sensitivity. However, current comparative reports are highly contradictory, attributed by a limited sample size and the use of different SM and MPF ELISA kits.
Therefore the aim of this study is to validate MPF as a MPM biomarker, and to establish which marker is more sensitivy by comparing their diagnostic performance.
**Materials and Methods:** Serum from 408 study participants, enrolled in 6 cohorts, healthy controls ($n = 77$), healthy asbestos-exposed individuals ($n = 85$), patients with benign asbestos-related disease ($n = 102$), benign respiratory disease ($n = 46$), lung cancer ($n = 53$) and MPM ($n = 45$), was analyzed for SM and MPF concentrations using the MesomarkTM and Human MPF ELISA kit, respectively.
Biomarker levels are logarithmically transformed to apply parametric tests. Comparison of means was performed with one way analysis of variance (ANOVA) and post hoc multiple comparisons were done using the Bonferroni correction. Pearson's analysis determined the correlation between markers. Diagnostic performance was assessed with receiver operating characteristics (ROC) curve analysis and area under curve (AUC) values.
**Results:** SM and MPF levels differentiated MPM patients significantly from each cohort ($p < 0.001$) and both markers were highly correlated in MPM patients ($r = 0.869$, $p < 0.001$). ROC curve analysis for SM and MPF did not reveal a significant difference in AUC values (SM = 0.888 versus MPF = 0.881; $p = 0.756$) for distinguishing MPM from all cohorts. However, at 95% specificity, the sensitivity of MPF (78%; cut-off = 12.76 ng/mL) was superior to SM (64%; cut-off = 2.00 nmol/L). In addition, SM did not add information concerning the presence of MPM, compared to the use of MPF alone, and diagnostic performance did not improve by combining both markers.
**Conclusion:** MPF was validated as a performant MPM marker in the largest cohort study so far. In addition, at the same specificity, MPF had a superior sensitivity than SM. As such, we argue that MPF has the potential to become the marker of choice in MPM management.