Results: In the whole population, CDA Lys27Lys polymorphism significantly correlated with better response (P=0.04) and higher haematological toxicity. In the cisplatin/gemcitabine-treated patients, significant correlations were observed between CDA Lys27Lys genotype and better response, grade >3 neutropenia, as well as with longer TTP and OS (P=0.01 and P=0.001, respectively) (Table 1).

Table 1. Correlation between CDA 27 genotype SNP and activity, efficacy and haematological toxicity of chemotherapy.

	CDA Lys27Gln			
	Lys/Lys	Lys/Gln	Gln/Gln	p
Partial Response (%) (all 78 pts)	50.0	26.2	12.5	0.04
TTP (months) (all 78 pts)	7.0	4.4	5.0	0.10
TTP (months) (52 Cddp-Gem treated pts)	8.0	5.5	2.0	0.01
OS (months) (all 78 pts)	18.8	9.9	NA	0.26
OS (months) (52 Cddp-Gem treated pts)	22.5	14.3	6.7	0.001
Neutropenia G≥3 (%) (all 78 pts)	39.3	4.8	0.0	0.0003
Thrombocytopenia G≥3 (%) (all 78 pts)	25.0	7.1	0.0	0.04
Anaemia G>3 (%) (all 78 pts)	0.0	4.8	12.5	0.24

G, grade; NA, not assessable

The multivariate analysis confirmed the prognostic significance of this polymorphism (P=0.02), while no significant associations were found among ERCC1 and XPD polymorphisms and clinical outcome in this group of patients. CDA genotype didn't result predictive of response and toxicity in patients treated with gemcitabine alone.

Conclusions: CDA Lys27Gln polymorphism resulted a predictive biomarker of response rate, toxicity, TTP and OS in advanced NSCLC patients treated with cisplatin and gemcitabine, thus offering a potential new tool for treatment optimization. Enzymatic activity assays on blood samples are ongoing to better understand this feature.

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D3-07 Pharmacogenomics & Biomarker in Cytotocix Chemotherapy, Thu, 12:30 - 14:15

SNP of Phospholipase D1 gene as a Predictive Marker for Response to Chemotherapy in Non-small Cell Lung Cancer

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Background: Phospholipase D (PLD) is activated by stimulators of vesicle transport, endocytosis, exocyosis, cell migration, and mitosis. These cellular biological processes are deregulated in the development of various human tumors. The involvement of PLD in tumorigenesis suggests that PLD could be valuable targets for therapeutic intervention and phamacogenetics focuses on the prediction of the effect of chemotherapy by genetic profiling in cancers. Single nucleotide polymorphisms (SNPs) are extensively used in case-control studies of practically all cancer. The identification of polymorphisms of cancer patients may help the clinician prescribe the optimal drug combination or schedule and predict the response of chemotherapy with accuracy.

Method: The purpose of this study was to analyze genetic polymorphisms of phospholipase D1(PLD1) gene as a predictive marker for response to chemotherapy in non-small cell lung cancer.

Results: We identified two SNPs at the exon 14, one SNP at the exon 16 and six SNPs at the exon 23. cSNPs of PLD1 was selected according to the degree of heterozygosity; (exon 23, rs2668, allele A/C: A2668C). The allelic frequencies of A2668C was 70.85 % in 211 non-small lung cancer patients. The allelic frequencies of A2668C polymorphism of responders (partial response) showed significant association with non-responders (stable disease and progression) to chemotherapy (p=0.059, OR=1.739). Also, the genotype frequencies of A2668C polymorphism of responders showed significant association with non-responders to chemotherapy (p=0.017, OR=2.198). Between gender and smoking on the risk of lung cancer, significant association was found in genotype frequencies of A2668C polymorphism (p=0.013, OR=2.651).

Conclusion: From our results, we suggest that PLD1 genetic polymorphism (A2668C) might be a predictive marker for response to chemotherapy in non-small cell Lung cancer.

Session D4: Pathology

Thursday, September 6

D4-01 Pathology, Thu, 12:30 - 14:15

Correlation between high-resolution CT findings, histopathological and clinical findings of small pulmonary adenocarcinomas

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Background: Previously, we reported that small pulmonary adenocarcinomas (tumor diameter 20mm or less) could be classified according to attenuation on high-resolution CT (HRCT) images as either 'air-containing type' ('fair-type') or 'solid-density type' (='solid-type') (Lung Cancer 36 (2002)). Air-type was defined as having areas where tumor opacity on mediastinal window images were half or less than half the size of those noted on lung window images. Solid-type was defined as having areas where tumor opacity on mediastinal window images was greater than half the size of those noted on lung window images. Our findings indicated that there was no microscopic evidence of metastasis with air-type nor any relapses nor deaths, after resection. By contrast, patients with solid-types demonstrated a poor prognosis. At this time, the histopathological characteristics of areas of tumor opacity noted on mediastinal window images have not been fully investigated.

Method: We retrospectively reviewed the records and CT scans of 118 patients, who had undergone surgical resection of peripheral adenocarcninomas. All tumor diameters were 20mm or less in size. All 118 patients had undergone HRCT prior to surgery. HRCT Images were acquired by a model X-Vigor/Real or an Aquillion CT scanner (Toshiba Medical Systems). High-resolution images of tumors were obtained at 135kVp at 250mAs with 1-2mm section thicknesses. All images were photographed using mediastinal (level, 40HU; width, 400HU) and lung (level, -600HU; width, 1600HU) window settings. We analyzed the correlation between areas of tumor opacity of mediastinal window images and the histopathological and the clinical findings.

Results: Areas of tumor opacity noted on mediastinal window images demonstrated five possible histopathological findings; 1. collapse (C),

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