Detection of Chromosomal Instability by Fluorescence in Situ Hybridization in Surgical Specimens of Non-Small Cell Lung Cancer

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**Purpose:** The aim of this study was to evaluate prognostic importance of chromosomal instability (CIN) in non-small cell lung cancers (NSCLC). We examined the relationship between CIN detected by fluorescence in situ hybridization and survival in patients with NSCLC and subgroup.

**Experimental Design:** 132 surgical specimens of NSCLC were studied. The patients included 109 men and 23 women, with a median age of 59 years. Tumors included 64 adenocarcinomas (AC), 68 squamous cell carcinomas (SCC). The pathologic stage was IA in 22, IB in 53, IIA in 5, IIB in 28, IIIA in 18, and IIIB in 6 cases. Multi-target DNA FISH assay (LAVision, Vysis) was used to determine which tumors carried CIN. Survival were compared according to the following factors: gender, age, histology, T factor, N factor, CIN and smoking status.

**Results:** Fifty tumors (37.9\%) showing numerical heterogeneity in all four examined chromosomes were judged to be carrying CIN. The percentage of CIN was significantly higher in Adenocarcinoma group than squamous cell carcinoma group. (54.7\% vs 22.1\%, $p<0.001$) The rate of lymph node involvement was lower in CIN positive group. (26\% vs 43.9\%, $p=0.039$) The CIN positive group had lower smoking history. (26.0 ± 24.0 vs 35.1 ± 24.2, $p=0.036$) In multivariate analysis, there was no significant differences two groups. Kaplan-Meier survival curves according to CIN status shows no significant differences. Log-rank test revealed only gender factor predicted a poor survival.

**Conclusions:** Our study demonstrates that CIN is more frequent in AC than SCC. But CIN is not an independent prognostic factor in the group of patients with NSCLC and in the subgroups: both with AC and SCC.

### P2-069

**A Retrospective Clinicopathological Study of the Epidermal Growth Factor Receptor (EGFR) profile in patients with resectable non small cell lung cancer**

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**Background:** Lung cancer is the biggest cause of cancer death in the US and Europe. Recently an increased understanding of the molecular biology of Non-small cell lung cancer (NSCLC) has led to the introduction of novel targeted therapies. The epidermal growth factor (EGFR), commonly overexpressed in NSCLC has emerged as an attractive target. This has led to the development of the EGFR tyrosine kinase inhibitors (TKIs) Erlotinib and Gefitinib and the monoclonal antibody directed against the EGFR, cetuximab. Other agents targeting the EGFR are in various stages of development. Several studies have shown that patients with somatic mutations in the EGFR TK domain are more sensitive to TKIs while mutations in K-ras, a mediator of EGFR signalling, are associated with resistance. Overexpression of the EGFR, detected by immunohistochemistry does not predict response to anti-EGFR therapy. Determining gene copy of the EGFR using fluorescent in situ hybridisation (FISH) appears to predict response to the TKI’s. Determining gene copy number of the EGFR using RT-PCR technology is not well explored and the prognostic value of this is as yet unknown.

**Aim:** The natural history of these mutations is unknown therefore the aim of this study is to examine a cohort of 200 patients who underwent resection for NSCLC, between 2002-2004 in St. James’Hospital, for EGFR/K-ras mutational status and EGFR amplification and expression.

**Methods:** DNA is extracted from the paraffin-embedded tumour tissue of each patient. Exons 19 and 21 of the EGFR gene and exon 2 of the K-ras gene are amplified using nested PCR. The PCR product is bidirectionally sequenced using BigDye Terminator v3.1 on the ABI 3100 sequencing instrument. The DNA is also subjected to quantita-