Abstract Group: 11.1. Lung Cancer

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Title: A detailed immunohistochemical analysis of PI3K/AKT/MTOR pathway in lung cancer: Correlation with PIK3CA, AKT1, K-RAS or PTEN mutational status and clinicopathological features

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Body: Objectives:1)To search for any relation between the mutational status of tPIK3CA,K-RAS,AKT-1 and PTEN and expressions of p85a and p110γ subunits of PI3K, phosphorylated (-)AKT,p-mTOR,PTEN,PP79S6K and p-4E-BP1 in non small cell lung cancer(NSLC).2)To correlated them with clinicopathological parameters. Methods:Retrospective study in 102 NSCLC patients. Expression of phosphorylated (p-)mTOR,p-AKT,p85a and p110γ subunits of PI3K,p-p70S6K, PTEN,p-4E-BP1 was studied by immunohistochemistry in 102 lung specimens. and correlation with clinicopathological features. Also 61 cases were tested for PIK3CA, AKT-1, PTEN and K-RAS mutations. Results:Patients were 14 females and 88 males(mean age 71years).18.5% of cases had a K-RAS mutation at codon 12, 5 had PTEN mutation(exon 7,8) and 1 had AKT-1 mutation (p.E17K). PTEN mutations were correlated with nodal metastasis. p-mTOR and p110γPI3K expressions were higher in adenocarcinomas and p-4E-BP1 in squamous carcinomas. An inverse correlation was noted between p-4E-BP1 immunoexpressin and tumour status and and nuclear p-AKT expression regarding stage. p-4E-BP1 expression single or combined with cytoplasmic p-AKT expression had an adverse prognostic significance in adenocarcinomas (univariate survival analysis). Conclusions:Alterations of PI3K/AKT/mTOR pathway are differentially implicated in the pathogenesis and aggressiveness of NSCLC. Nuclear p-4E-BP1 immunoexpression seems to be a prognostic molecular marker in adenocarcinomas especially when combined with p-AKT. Careful evaluation of these parameters may predict tumours most sensitive to PI3K/AKT signalling inhibitors.