Poster Session (Poster presentations categorized by each organ)

P2 – 26 – 3  EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) DEPHOSPHORYLATION AND GROWTH INHIBITION BY VINORELBINE IN EGFR-MUTATED CELL LINE

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Background: EGFR-tyrosine kinase inhibitors (TKI) often provides dramatic response to lung cancer harboring EGFR-activating mutations, but most patients eventually fail these treatment. We have reported the efficacy of vinorelbine (VNR) and dihydropyrimidine dehydrogenase (DPD) inhibitory fluoropyrimidine (DIF) for advanced non-small cell lung cancer patients, in particular EGFR mutant lung adenocarcinoma. The aim of this research was to elucidate the mechanism of efficacy of vinorelbine and DIF to EGFR mutant lung adenocarcinoma.

Methods: We used a PC9 lung adenocarcinoma cell line with EGFR-activating mutation, and evaluated whether VNR or 5FU affect the phosphorylation of EGFR using Western blotting. Then, we transfected mutated EGFR gene to IBR3 fibroblast cell line and measured the sensitivity of VNR to IBR3 with or without transfection of mutated EGFR.

Results: In PC9 cells, VNR induced dose- and time-dependent dephosphorylation of EGFR at clinically achievable concentrations, but 5-FU did not. EGF phosphorylated EGFR and reduced the sensitivity of PC9 cells to VNR. Sodium vanadate induced sustained phosphorylation of EGFR, and also conferred resistance to VNR. The sensitivity of VNR to IBR3 cells transfected with mutated EGFR was higher than that of the parental IBR3 cells.

Conclusions: We showed that VNR inhibits proliferation of EGFR-mutated cells through EGFR dephosphorylation.