**IMPACT OF STATINS FOR THE TREATMENT OF NON-SMALL CELL LUNG CANCER**

C. Minichsdorfer¹, D. Aydemir²

¹Department of Medicine I, Medical University of Vienna, Vienna, AUSTRIA
²Oncology, Internal Medicine I, Vienna, AUSTRIA

**Aim:** Lung cancer is still the leading cause of cancer mortality world-wide. Erlotinib is a novel EGFR tyrosine kinase inhibitor that has shown promising results in the treatment of patients with advanced NSCLC. HMG-CoA reductase inhibitors (statins) have shown promising in-vitro activity against a large number of tumour cell lines. However, most statins are metabolized in the liver by CYP3A4 and therefore can lead to severe drug interactions when co-administered with drugs using the same pathway, like erlotinib. Fluvastatin and pitavastatin are metabolized by different pathways and are therefore no matter of drug interactions with erlotinib. Aims of this study were to investigate the cytostatic effects of fluvastatin, pitavastatin and simvastatin alone and in combination with erlotinib on 6 different NSCLC cell lines.

**Methods:** Experiments were carried out with human NSCLC cell lines A549 (K-RAS mutation), Calu-6 (K-RAS mutation, F53 mutation), H1650 (EGFR mutation, erlotinib resistant), H1975 (EGFR mutation, erlotinib resistant), HCC 827 (EGFR mutation, erlotinib sensitive), H1993 (MET oncogene amplification). We investigated the activity of caspase 3 upon statin treatment by cleavage of specific fluorescent caspase substrates. Inhibition of growth was assessed by MTS assays.

**Results:** Statins lead to growth inhibition in all 6 NSCLC cell lines investigated in a dose dependent manner. Our data indicate that A549 and Calu-6 cells which harbour K-RAS mutations are most susceptible for this statin effect. Moreover statins induce caspase 3 activation which is accompanied by morphological changes typical for apoptosis. Interestingly, K-RAS mutated cells showed increased sensitivity to statins. Strikingly the combination of erlotinib and pitavastatin proved to be more effective in NSCLC cells harbouring K-RAS mutations, as this treatment led to a more pronounced inhibition of growth in contrast to each drug alone. A trend to additional effects was observed in H1650, H1975 and H1993 cells however, these effects were not statistically significant.

**Conclusions:** Our data indicate, that especially NSCLC cell lines with K-RAS mutations are most susceptible to statin induced apoptosis and growth inhibition. Furthermore co-treatment with statins led to a higher sensitivity to erlotinib in K-RAS mutated cell lines.

**Disclosure:** All authors have declared no conflicts of interest.