

## Summary

### USE OF TUMOR MARKERS IN POSTOPERATIVE PROGNOSIS OF NON-SMALL-CELL LUNG CANCER

#### Introduction:

The most frequently used prognostic parameters in clinical practice of NSCLC are disease stadium and affection of hilar or mediastinal lymph nodes. These phactors are not sufficient and therefore new prognostic parameters - tumor markers - are being searched for. Tumor markers regarding NSCLC have mainly been used so far to monitore effects of medical treatment or detection of carcinoma recurrency. The study concentrates on assessment of tumor markers signficance for NSCLC.

#### Methods:

The total group includes 125 patients operated on for NSCLC in the years 2004-2007. Single groups of patients were assessed successively. Serum markers CYFRA 21-1, CEA, TK, TPS, and NSE were assessed in an immunoanalytical way in 34 patients: Serum parameters of angiogenesis through Luminex<sup>®</sup> xMAP<sup>®</sup> technology were assessed in 27 patients. Serum values of cytokeratins were assessed in an immunoanalytical way with 125 patients. Expressions of metalloproteinases (MMP-7, MMP-9) and their inhibitors (TIMP-1, TIMP-2) were assessed in NSCLC tissue with 91 patients and in lung tissue with 12 patients with benign pulmonary disease. Finally, OS and DFI were assessed in accordance with tissue expression of metalloproteinases and their inhibitors with a group of 76 patients. Comparison was executed in clinical groups of progression and remission.

#### Results:

A year or longer time after a surgery, p-values, values of differences of serum values of given markers between remission and progression groups are following: for TK=0,0176 for TPS=0,0378 and for CYFRA 21-1=0,0179. A significant difference was detected in serum values of the remission group patients compared to the progression group of patients for the cytokeratin marker MonoTotal (p= 0,0077). In the adenocarcinoma group there was a significant difference of median values (p< 0,05) detected compared to the group of benign pulmonary disease patients. Significant are differences of both absolute and normalized values of the tissue expressions of MMP-7 and TIMP-1 (p=0,003; 0,0018 resp.) between NSCLC tissue and benign lung tissue. The expression value of TIMP-2 of squamous form of NSCLC tissue taken during a surgery is a statistically significant (p=0,0398; 0,0500 resp.) factor of disease free interval, whereas other assessed parameters are not.

#### Conclusion:

Regarding all the tested markers, the most clinically significant are classical tumor markers, predominantly CYFRA 21-1, recently MonoTotal (sensitive for squamous carcinoma), and CEA (for adenocarcinoma). Other significant markers are TK and TPS which show fast and dynamic changes according to clinical state. This study confirms the significance of metalloproteinases (MMP7, MMP-9, and TIMP-1 and TIMP-2) from the point of view of growth and progression of NSCLC. Rapid growth of TIMPs (mainly TIMP-2) expression makes these markers promising for future research.

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