Lung cancer is the most frequent malignancy in terms of cases and deaths number. Each year over 22000 patients in Poland fall in that disease and it is equal to the number of inhabitants in such Polish cites as Kętrzyn, Jarocin, Hajnówka, Andrychów or Augustów, or Swiss Baden, or the whole San Marino. Lung cancer is mainly caused by tobacco smoking habits, which is the reason of many diseases of respiratory and cardiovascular systems, but also by late disease diagnosis, which excludes the possibility of effective treatment. Therefore, the mortality rate of lung cancer is extremely high and amounts 86%.

Late diagnosis of lung cancer cause a main issue in treatment of the disease. The late diagnosis is caused by asymptomatic tumor grow leading to discrete symptoms like hoarseness, weakness or decrease in physical condition, which are often ignored by patients. Therefore, the lung cancer is commonly diagnosed in advanced stages and the vast majority of patients will develop distant dissemination, including 20-40% who develop brain metastases. Owing to protective function of blood-brain barrier, brain metastases are resistant to most cytotoxic agents used in chemotherapy. Therefore, the management of BM includes neurosurgery, radiosurgery, whole brain radiation therapy. Molecularly targeted therapies, matched to the intracellular pathways proteins which are the products of mutated genes, may give new treatment possibilities of brain metastases.

Molecularly targeted therapies have shown relatively high activity in non-small cell lung cancer patients harboring *EGFR* gene mutations, as well as *ALK* and *ROS1* genes rearrangement, which occur in 10%, 5% and 1% of Caucasian patients, respectively. These genetic abnormalities are more commonly detected in non-smokers and in adenocarcinoma patients. Recently, the application of next generation sequencing technique have provided a wide array of data on the molecular background of lung cancer (many thousands of mutations in tumor suppressor genes and oncogenes). It may result in extension of possibilities for patients' qualification to novel molecularly targeted therapies and immunotherapies which are based on a new agents.

Clinical data suggest, that molecularly targeted therapies show a promising activity also in brain metastases of lung cancer. However, there are relatively a few clinical trials matched to them. Moreover, insufficient knowledge about molecular background of brain metastases, as well as a genetic heterogeneity between primary tumor and corresponding metastatic lesions limited wide application of molecularly targeted therapies for brain metastases of lung cancer. Therefore, most of patients is treated only using radiotherapy or neurosurgery.

Molecular abnormalities in brain metastases of lung cancer may influence on effectiveness and safety of treatment. Therefore, in following proposal we assume a comprehensive analysis of the molecular background in brain metastases using next-generation sequencing techniques. Moreover, we plan to compare genetic variation between metastatic and corresponding primary lesions. We will also correlate the occurrence of molecular abnormalities with activation status of immunology system, which could control the development of tumors. It is expected that this study will provide new data on the pathogenesis of BM in lung cancer and pave the way for further translational and clinical research allowing the development of novel diagnostic and therapeutic approaches in advanced stages of lung cancer.