Usefulness of “liquid biopsy” in diagnostics, stratification, and monitoring of therapy in non-small cell lung cancer patients

Despite advances in the detection and treatment of non-small cell lung cancer (NSCLC), nearly half of the patients have metastatic disease at diagnosis, which significantly reduces the chance of successful treatment. This is because the symptoms of lung cancer at the early disease stage are subtle and non-specific. Moreover, there is no effective method of early detection of NSCLC, when the chances of a successful treatment are the highest. So far, the greatest achievement in the detection and treatment of NSCLC is the so-called personalized medicine. It is based on an individual approach to the patient and tailoring the treatment to a specific person. In the case of NSCLC, it is based on a combination of two approaches - the assessment of a biopsy, based on the collection of tumor tissue fragment or metastasis, and the determination of mutations, which are specific changes in the patient's DNA. Analysis of mutations in the EGFR gene allows the use of so-called targeted treatment, e.g., treatment adjusted to a specific patient's needs. The downside of this approach is that the tumor has a diversified composition, not always allowing for mutation detection.

A promising solution seems to be the detection and characterization of circulating tumor cells (CTCs). These are the cells that circulate in the bloodstream after detaching from the primary tumor and can lead to metastasis. The assessment of their number and changes in DNA could, therefore, allow the determination of the stage of the disease, the selection of individual therapy, and the control of treatment effects. However, the biggest challenge is successful isolation of these very rare cells from the blood of cancer patients. The most common and recognized technique for detecting them is the CellSearch® system. It detects cells on the basis of the presence of the EpCAM molecule on their surface, specific for carcinomas. However, CTCs in the bloodstream change from epithelial to connective tissue character. It leads to the loss of the EpCAM molecule, and thus the CellSearch® method ineffectiveness.

This is also the common problem in NSCLC, and despite the very aggressive nature of the disease, the number of cells presenting the EpCAM molecule is low. This does not mean that there is no CTCs in the bloodstream, it only indicates the presence of an altered population.

Therefore, the project will aim to create a new, precise diagnostic method that will be used for the early detection of non-small cell lung cancer. The study will include patients with NSCLC adenocarcinoma, qualified, based on genetic testing, for treatment with tyrosine kinase inhibitors. All analyzes will be performed twice - before the therapy and 10-14 months after its start. The choice of the above time point is based on the data showing that, at this time, treatment resistance is most common.

The research will be based on the use of an alternative technique of CTC detection in NSCLC - EpCAM-independent EPISPOT method. It is based on the detection of viable cells as the only ones that can lead to metastasis. Moreover, cells obtained by this method can be subjected to mutation assays. An additional element of the research will be the analysis of free-circulating DNA (cfDNA) released from cells and isolated from patients' serum. It has been shown that, like CTC, it can be a good source of information about mutations in tumor cells. Both elements can be classified as "liquid biopsy," which is a non-invasive alternative to standard tissue biopsy.

The usefulness of the "liquid biopsy" in the detection of NSCLC, selection of the appropriate therapy, and its monitoring will be assessed by comparing the effectiveness of CTC detection by both tested methods, determining the convergence of the "liquid biopsy" mutations in relation to the tumor tissue and the correlation of the obtained results with the patient's clinical condition and results of routine diagnostics.

The most important expected results include the demonstration that the components of "liquid biopsy" are a good alternative to the classic tissue biopsy and allow for the assessment of the patient's clinical condition, stratification of the patients to the appropriate type of treatment, and effective control of the therapy course.