The use of genetic analysis of liquid biopsy for predicting and monitoring of response to therapies and tumor evolution in patients with melanoma

Melanoma is the most aggressive skin cancer that spreads very quickly from its original location to the rest of the organs. Patients with disseminated melanoma are treated with two types of therapy: BRAF and MEK mutant protein inhibitors and immunotherapy. These two types of drugs have significantly prolonged the survival of patients with advanced melanoma, and now patients with stage IV melanoma can live more than two years. This applies, however, only to some patients. More than half of the patients die during the first three years of therapy due to the further progression of the neoplastic disease. The ability to predict whether the patient will benefit from the proposed therapy and to quickly detect disease progression during treatment would allow better treatment planning, save the patient from unpleasant side effects of therapy, and reduce costs. Genetic analysis of the liquid biopsy is one of the potential tools for predicting and monitoring response to therapy, as well as identifying new therapeutic targets. It is a test that can identify the individual genetic characteristics of a patient's cancer and determine the severity of the disease, all in a single blood sample.

In this project, we plan to investigate whether the genetic tests we have developed will allow us to predict the effectiveness of the proposed therapy before its initiation, and will quickly show during the treatment whether the drugs used are working. For this purpose, we would like to conduct four tests: (1) analyze the melanoma DNA circulating in the blood of patients for the presence of mutations in selected genes and determine the so-called "genetic signature" of cancer; (2) in selected 30 patients, we want to study this signature during treatment, observe how the genetic characteristics of the melanoma change and identify those mutations responsible for the resistance to treatment. We also plan (3) to determine the amount of mutated melanoma DNA in the patient's blood during treatment and to check whether this parameter is a good indicator of the tumor size, and thus the effectiveness of the therapy. In addition (4) we would also like to compare the genetic signature obtained in the blood test (liquid biopsy) with the signature obtained in the tumor test (the standard biopsy) and check whether the easier, cheaper, and repeatable liquid biopsy test can replace the analysis of the tumor material. We plan to conduct experiments on approximately 180 patients with advanced melanoma treated in the Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch.

The implementation of this project will answer the question of whether our genetic test performed in a liquid biopsy will predict how the patient will respond to the treatment, and whether the therapy is working and, if not, what genetic features of the tumor are responsible for it. The use of such a test in clinical practice would allow better adjustment of the therapy to the patient's cancer, and in case of failure, it would be possible to quickly identify other potentially effective drugs.