Lung cancer is the most frequently diagnosed neoplasm and the most common cause of cancer death in Poland; approximately 85% of all diagnosed cases are non-small cell lung cancer. Treatment options, especially in the advanced stage of the disease, are limited. However, the advent of so-called immune checkpoint inhibitors, drugs that suppress the effects of cancer on the immune system, has led to a significant improvement in the treatment results. Despite impressive treatment responses leading to long-term survival for some patients, not all benefit from this type of therapy. The reasons are largely unknown, but it is recognized that the tumor microenvironment, including the expression of immune suppressing molecules (PD-L1 protein) and the lymphocyte populations within the tumor, has a significant impact on the response.

One strategy to increase the proportion of responders is the combination of immunological drugs with conventional cytotoxic treatment - systemic (chemotherapy) or local (radiotherapy). Although preclinical and animal studies suggest potential for synergistic effects of such a combination by the induction of PD-L1 protein expression by chemo/radiotherapy and the infiltration of lymphocytes into the tumor, the results of clinical trials assessing the effectiveness of this combination are inconclusive. One reason may be our insufficient understanding of the immune response to DNA damaging drugs in humans.

Hence, the aim of the proposed study is to comprehensively assess the interaction between the cancer and the immune system in non-small cell lung cancer. We plan to recruit patients whose clinical situation makes tumor resection within 4-5 weeks of completion of chemo- or radiochemotherapy the optimal treatment. This way, the amount of tumor tissue that has been treated with cytotoxic agents available for evaluation will be relatively large and will allow in-depth molecular investigation. In addition to assessing the expression of immune inhibitors, tumor mutational burden which is associated with increased tumor immunogenicity and infiltration by various lymphocyte populations, we also plan to assess the expression of a panel of genes relevant to the phenomenon under study. The planned study will therefore enable the identification of key genetic, immunological and molecular aspects determining the response to immunotherapy. Assessment of the expression of inflammatory cytokines and microRNAs in the serum of patients at several time points will allow us to assess the relationship between immune phenomena inside the tumor and in the peripheral blood, which may contribute to increasing the knowledge of biomarkers useful in selecting the appropriate therapy and monitoring treatment results in non-small cell lung cancer patients.