In Poland, cancers of the head and neck (HNC) account for 5-6% of all malignancies. Nearly 75% of HNC patients are diagnosed at advanced stage and, in most cases, radiotherapy (RT) and cisplatin-based chemoradiotherapy (CHRT) are the treatment of choice for these patients. In addition, both RT and CHRT, enable function and organ preservation, offering comparable effectiveness to surgical treatment. However, despite advances in diagnosis and therapy, the treatment outcome is unsatisfactory and prognosis in locally advanced HNC remains unfavorable. Five-year survival is approx. 50%, and the rate of failure and local recurrence exceeds 50%, while 20-30% of patients develop distant metastases. A common phenomenon is the occurrence of a second primary malignancy. Moreover, RT and CHRT are inevitably accompanied by side effects that may cause a dose reduction or unplanned treatment interruption resulting in treatment failure. Post-treatment quality of life of the patients is often reduced due to long-term complications of RT and CHRT which may lead to shorter survival.

Therefore, the urgent need in the treatment of HNC patients is to find reliable predictive and prognostic markers of response to RT and platinum-based CHRT that could help planning and optimization of treatment in order to reduce the risk of complications, recurrence and metastasis. Currently, the factors determining the choice of treatment include clinical and pathological stage, lymph node status, histological grade, tumor localization and general condition of the patient. However, they do not allow to estimate accurately the expected therapy effects and predict the course of the disease, while patients with similar clinicopathological characteristics treated in the same manner show significant differences with regard to the outcome. A solution to this problem is seen in the search for biological markers at the level of patient' genome. Many reports (including the work of our team) show that one of the key factors affecting the effectiveness of anticancer therapy and prognosis is genetic background of the patient (host genetic factors), determined by i.e. multiple single nucleotide polymorphisms (SNPs). Research on the role of SNPs as potential prognostic and predictive factors in cancer is an interesting and developing area of knowledge. It has been shown that various SNPs may modulate DNA repair capacity, efficiency of drug biotransformation and transport, antioxidant enzymes activity and even the ability to metastasize as well as to form new blood vessels. At the molecular level, this phenomenon is complex and poorly understood, while the existing data are scarce, conflicting, often based on analysis of small and/or heterogeneous patient groups. Majority of these studies remain unverified. In HNC, the attention of researchers has focused mainly on the relationship between SNPs and risk as well as severity of radiation adverse effects, but relatively little information is available on the prognostic significance of SNPs in genes involved in mechanisms essential for action and effectiveness of ionizing radiation (IR) and cisplatin, such as DNA strand breaks repair, enzymatic antioxidant defense or angiogenesis. Thus, the assumption of the proposed project is that some functional or potentially functional SNPs in selected genes, leading to changes in levels and activity of the encoded proteins, may modulate individual sensitivity to IR and cytotoxic drugs, which is then reflected in diverse anticancer therapy results, risk of progression and survival in HNC patients.

Thus, the main objective of the project is to assess whether certain polymorphic variants in selected genes are associated with therapy outcome, including response to treatment, risk of recurrence and metastasis as well as patient survival, in head and neck squamous cell carcinoma (HNSCC) treated with RT and cisplatin-based CHRT. We will analyze SNPs that are very poorly studied or not examined so far in HNC. Their potential influence on clinical outcome will be verified in a group of at least 500 HNC patients. The additional aim is to create an extensive, very well characterized clinically and molecularly, collection of biological material of HNC patients that will serve as a basis for future research.