

## STRESZCZENIE W JĘZYKU ANGIELSKIM

Melanoma is a malignant tumor that originates from melanoblasts - precursors of pigment cells of neuroectodermal origin, migrating to various tissues from the neural tube in the early period of embryonic development. The starting point of most melanomas (about 90%) is the skin. Until recently, the prognosis in patients with advanced clinical stage of melanoma was poor, and the 5-year survival rates were 5-10%. A breakthrough in the treatment of melanoma patients was the introduction of ipilimumab, a recombinant human monoclonal antibody of the IgG1 subclass that binds to the CTLA-4 receptor. The CTLA-4 antigen, along with the CD28 glycoprotein found on T lymphocytes and CD80 and CD86 ligands present on the surface of APC, are the most important particles involved in the so-called 2nd cost-stimulating signal of T lymphocyte activation. In the following years, new treatment options appeared, both targeted to signal transduction molecules (BRAF and MEK inhibitors) and immunotherapy with anti-PD-1 antibodies (nivolumab, pembrolizumab), as well as combinations of the above treatment methods. In this situation, it becomes necessary to personalize treatment and select groups of patients who will benefit most from a given therapy. An attempt to determine one of them was made in this doctoral thesis.

The aim of the study was to try to find predictive factors for ipilimumab therapy. Currently, treatment with ipilimumab remains the standard in the first-line therapy of patients with advanced melanoma as a component of doublet immunotherapy, together with anti-PD-1 antibodies. Finding predictive factors for anti-CTLA-4 therapy would allow to select patient with an expected response to such treatment and to avoid complications in patients whose prognosis is not improved by such therapy.

In this study, the serum of 37 patients with advanced melanoma qualified for ipilimumab treatment under the extended drug access program was tested. Blood serum was collected before starting immunotherapy. The parameters assessed in the laboratory were the soluble forms of components 2nd of the co-stimulating signal of T lymphocytes of the CD28 family: sCD28, sCD80, sCD86. The results of the measurements of the above parameters in the blood serum were then correlated with the overall survival time (OS) of the patients as the most important parameter proving the effectiveness of the therapy. Statistically significant differences in overall survival between the groups with low sCD86 and high sCD86 concentrations in favor of the first group were demonstrated. However, differences in baseline concentrations of sCD80 and sCD28 could not be related to the duration of OS.

Additional statistical analyzes were performed to assess the impact of demographic parameters and the course of the disease and treatment to the length of response to ipilimumab treatment in patients with advanced melanoma. According to the obtained results, a better response to treatment (in the form of a longer OS) was found in male patients, patients in very good general condition at the start of treatment (ECOG 0) and in fewer lines of chemotherapy (1 - 2 lines of treatment vs. more than 2 lines of treatment) used before immunotherapy. However, there were no differences in OS between patients with different locations of the primary lesion (limb location, central location), nor age at diagnosis of advanced cancer.

The above results open the way to in-depth research on the above parameters, but their final value as predictive factors and impact on the actual choice of therapy in patients with advanced melanoma requires confirmation of these conclusions in a larger group of patients.