DESCRIPTION FOR THE GENERAL PUBLIC

Plasma cell myeloma is one of the most common hematologic malignancies, which currently afflicts more than one million people worldwide. In Poland, more than 1,500 patients are diagnosed de novo each year. Nowadays, the number of patients living with myeloma in our country is estimated at about 8,000 people. Recently, the mean survival rate for PCM patients has increased nearly twice, and now it is about 7-10 years. Prolongation of life in this disease mainly results from the implementation the new drugs like proteasome inhibitors (bortezomib), as well as therapy using the allogeneic stem cel transplantation. Proteasome inhibitors are drugs of high activity in the treatment of patients with plasma cell myeloma. They are characterized by high selectivity towards myeloma cells and relatively fewer undesirable side effects, thus being very important elements of therapy. During treatment in myeloma cells appears mutations determining the resistance to proteasome inhibitors. Approximately 20% of patients exhibit primary resistance that determines lack of response to treatment. The rest of patients develop resistance at different stages of treatment. So far, these mutations have been selectively examined, usually using commercially available myeloma cell lines. Our planned study should comprehensively determine the presence of all previously described genetic disorders that may affect the resistance in patients with a clinically detected loss of response to the treatment. Research will be conducted on the myeloma cells isolated from the bone marrow several times: 1. prior to the treatment, 2. during relapse after the treatment with proteasome inhibitors and 3, after the retreatment with bortezomib or carfilzomib. On isolated myeloma cells following tests will be performed: post-translational modification increasing the expression of proteins β5 proteasome, POMP, NRF2, C-MAF and MAFB, Xbp1, loss of the chromosomal region 8p21, point mutations of the gene *PSMB5*, *XBP1*. It will be assessed the levels of cytokines in the clinical course of patients with diagnosed myeloma and also established miRNA profile.

The determination of genetic defects could be practically used in the patients with plasma cel myeloma in order to speed up and reduce the cost of the establishment of targeted therapy. The challenge the authors of the project face is not only scientific progress but also the ability to offer the results of this progress to the patients. Implementation of this project could have important scientific and practical implications, which would allow the researchers to create guidelines for the patients suffering from PCM in whom the resistance develops during treatment as well as to optimize the choice of therapy in patients with newly diagnosis of PCM. The existing state of knowledge on the research subject will contribute to solving the posed problem in this particular discipline in Poland and abroad.