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In the recent few years we observed a constant and difficult to explain increase of the incidence of malignancies originating from hematopoetic cells. Currently, chronic lymphocytic leukemia (CLL) – a tumor originating from B-lymphocytes is the most commonly diagnosed leukemia type. Major differences in the course of the disease are observed – while some patients with very low tumor progression do not require treatment, some suffer from galloping disease, develop drug resistance and need to be treated with multi-drug combinations. Due to advanced age of patients (in Poland the median age at the time of diagnosis is 72 years old), it is of utmost importance to create safe combination schemes with minor side effects. In recent years in hematologic community a question of chemotherapy-free therapy is continuously raised. Many doctors incline towards targeted therapy combined with specific inhibitors of cancer signaling pathways. However, the application of such drugs needs to be preceded by thorough studies at molecular level.

One of responses towards the concept of chemotherapy-free therapy is the clinical application of anti-CD20 monoclonal antibodies (mAbs). By recognizing CD20 membrane antigen the antibodies induce a cascade of mechanisms engaging immune cells to combat the tumor cells. The binding of the antibody to CD20 molecule results in death of tumor cell either by the action of complement cascade or programmed cell death. The therapy wirh anti-CD20 antibodies engages as well the mechanisms of innate immune response such as cytotoxic action of natural killer (NK) cells as well as phagocytosis i.e. engulfment and digestion of tumor cells by macrophages.

Anti-CD20 monoclonal antibodies are well-tolerated, have minor side-effects and are successfully incorporated into multidrug combination schemes. However, when used as single agents anti-CD20 mAbs are rarely reported to produce full recovery. Therefore, efforts to increase the efficacy of anti-CD20 antibodies by the use of rational combinations with other drugs used in oncology have constantly been made. The results of our studies, that have been published in international research journals, indicate that the use of some new compounds already registered or being still tested in clinical trials leas to sensitization of established tumor cell lines to anti-CD20 mAbs. Thanks to our collaboration with the Institute of Hematology and Transfusion Medicine in Warsaw we were able to prove our observations on the blood samples obtained from patients suffering from CLL. The next step of our project should therefore be the verification of our observations in animal model. This is indeed the aim of this project. We aim at creating murine models enabling us to assess the therapeutic potential of the proposed combinations in a complex manner. Murine models, even if they can only be viewed as approximation of reality, will allow us to identify positive and negative interactions within combinations previously tested in in vitro setting. Moreover, in this project we will create a specialized platform enabling the thorough assessment of parameters essential for the success of anti-CD20 therapy.

By combining data from in vitro studies and information provided by murine models we will acquire a deep view of the efficacy of the proposed combinations. Thus, the results obtained by us can serve as a rationale for testing the most promising combinations in clinical trials.