Description for the general public

Chronic lymphocytic leukemia (CLL) is the most common type of leukemia among the adult population in Europe and North America. It is estimated that 25-30 % of all leukemias cases are CLL. Annually, 3-4 new cases of CLL are diagnosed among 100 000 inhabitants. The disease affects mostly elderly population, with median age at diagnosis amounted to 72 years. Although the definition of CLL may suggest the chronic nature of the disease, CLL is characterized by considerable heterogeneity. Only 30% of patients live 10-20 years from the diagnosis. Others, despite the mild onset of the disease, in 5-10 years develops terminal phase. In the case of an aggressive form, the patients live 2-3 years after the diagnosis. Spontaneous regression CLL is rare. So far, the cause of diverse natural history of the disease remains unknown.

Recurrent viral and bacterial infections are a major clinical problem in patients with CLL, they are also a common complication of immunosuppressive therapy / immunotherapy. Recurrent infections often complicate and delay the process of treating the underlying disease, especially in elderly patients. Chronic antigenic stimulation induced by the reactivation of latent viral infections (CMV, HSV, EBV, VZV) and / or chronic / recurrent bacterial infections (especially Streptococcus pneumoniae) can lead to the development of "anergy" and the development of specific response, called "immune risk profiles" (IRP), observed frequently in the elderly. Chronic antigenic stimulation leads to the generation of "worn-out lymphocytes", the accumulation of dysfunctional, anergic, resistant to apoptosis and clonal deletion CD8+ T cells, and susceptible to apoptosis CD4+ T cells. The pathogenesis of these changes is not exactly known, probably has to do with involution of the thymus, scarcity of new “naïve” cells and the development of the IRP.

Our planned clinical studies are designed to assess whether recurrent / chronic infections induce IRP and "anergy resilience" in patients with CLL. The study will detect among patients with CLL persons with IRP and a reactivation of EBV as well as other "ubiquitous" viruses (CMV, HSV, VZV) and / or recurrent bacterial infections that may lead to the development of clinical complications of the underlying disease, and hampering its treatment. Implementation of the project can contribute to a substantial deepening of knowledge about the causes of heterogeneous course of CLL and the possibility of using immunomodulatory drugs, antiviral agents, and immunization in the treatment of these diseases. The vast majority of diagnostic tests for viral infections is conducted using serological methods, also in patients with secondary immune deficiencies (hypogammaglobulinemia), leading to unreliable and often false negative results. The use of our more sensitive methods based on molecular biology techniques, which are more effective in detecting infections, and the latest immunological methods to assess the immune profile will help to determine the immune phenotype predisposing to recurrent / chronic infections. The project will assess for the first time on such a large scale the relationship between infections and the progression / exacerbation of clinical symptoms of CLL, which may change the way of perception the causes of the development of leukemia, and in the future possibly other cancers, not only hematological.