Principles of treatments in malignant hemopathies

Contributed by: UTM, Titu Maiorescu University, Bucharest

From 2017-01-24 **to** 2017-10-01, Romania

Chronic Lymphocytic Leukemia (CLL), occurs in middle aged and elderly person, affecting men and women in report 2/1. Patients with minimal evidence of disease, ie, lymphocytosis only, are considered to be early stage of disease, while those demonstrating compromise of bone morrow function as anemia or thrombocytopenia, are in advanced stages. The mutant genes and deletions in CLL can be regarded as biomarkers proteomic and genomic profile individual in this type of leukemia.

Principles of treatments in malignant hemopathies

Chronic Lymphocytic Leukemia, (CLL) remains an incurable disease in patients who require therapeutic intervention. It is particularly interesting that, although known as a pathological entity and studied for decades, CLL remains an incurable disease in patients who require therapeutic intervention. While some patients had quickly disease evolution and with a final immediately, other patients can survive for years without even require treatment.
It is known that in the normal cells, the flux of glucose is directed in a path lipogenic de novo, which is regulated in part by the enzyme phosphoinositol-3 kinase (PI-3K) activation dependent on the ATP-citrate lyase (ACL). Some researches show that inhibition of ACL leads to a loss of B cell growth and viability of the cell, [Zaidi N et al. Cancer Res 2012]. Activation of the PI3K / Akt is perhaps the most common spontaneous lesion in human cancers. The drug Crizotinib, a tyrosine kinase inhibitor targeting the AKT showed a significant increase in progression-free survival of leukemia. CD28 receptor is a co-stimulating action to further activate the cascade PI3K / Akt / mTOR pathway, in particular, and provides a signal to the Glut1 expression. The control mechanisms T reprogramming cellular metabolic are now light, and many of these oncogenes are also crucial to drive the metabolic conversion of T cells, most notably the stimulation of proto-oncogene Myc, hypoxia, factor-inducible hypoxia, (HIF) the mTOR pathway [Sharm Pet al. Cell 2011].

International cancer research with the latest studies have shown that signaling lymphocyte B cell receptor (BCR) is regulated in part by the amount of cholesterol in the cell membrane. It has been found that statins (Lovostatin), pharmacological inhibitors of cholesterol synthesis, induce apoptosis of CLL cells in vitro and in vivo. In addition, ectopic expression of CD5 in B-cell line stimulates the transcription of genes involved in cholesterol synthesis [Tomowiak C et al. Medical Research 2012]. The protein p-53 plays an important role in the regulation of glycolysis that is proven, experimentally. By contrast, the mutant p-53 does not affect the GLUT1 and GLUT4 receptor activity. Increasing of amount p53 protein seems a solution for preventing or treating their tumors spread. Pharmaceutical products, Nutline-3 displaces p53 by MDM2 compete for binding. Also, it has been found that strong Nutline-3 induces apoptosis in cell lines derived from hematological malignancies and B-cell CLL, with frequent translocations 14q32- 17p with a good therapeutic response [Secchiero et al. Clin Cancer Res 2010]. Thus, T cell activation, as a result of receptor signaling antigen and CD28 co-stimulation of the dendridic cells is followed not only by the induction of genetic programs leading to proliferation and functional differentiation, but also by inducing a program inhibitor mediated receptor CTLA-4, which will eventually stop proliferation [Shi LZ et al. J. Exp. Med 2011].
Like T cell receptor CTLA-4, the receptor T cell, PD-1, is expressed only in activated T cells to stop their proliferation at a time, limiting the production of memory T lymphocyte type. However, in contrast to CTLA-4, PD-1 inhibits T cell responses by interfering with T cell receptor signaling, as opposed to out-competing CD28. In many laboratory researches, today here are ongoing clinical trials with anti-CTLA-4 (Ipilimumab) in treatment CLL. Combination therapy can improve the anti-tumor responses.

Contributor

Organisation

UTM, Titu Maiorescu University, Bucharest
Calea Văcăreşti no: 187
7000 Bucharest
Romania
Website

Contact

MD Aurelian Udristioiu
Tel.: +40723565637
E-mail
See more events from this contributor

Related information

Programmes H2020-EU.1.2.

Countries Romania

Subjects

Scientific Research

Keywords

Chronic Lymphocytic Leukemia, P-53 gene, FISH, Cancer

Last updated on 2017-04-13

Category: Event
Provider: WIRE
Revision: 2
Retrieved on 2017-04-14

Permalink: http://cordis.europa.eu/event/rcn/149796_en.html