Abstract

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Title of diploma thesis: Effect of a new FLT3 inhibitor on induction of cell death in leukemia cell lines

Approximately 30% of patients with acute myeloid leukemia have a Flt3 kinase mutation, which is clearly a negative prognostic factor of the disease. Therefore, the development of new Flt3 inhibitors represents a major advance in the therapy of AML in these patients. Although standard treatment with chemotherapeutics (cytarabine and anthracycline) and allogeneic stem cell transplantation, which have been used in AML therapy for the past 40 years, lead to complete remission in many cases, they do not reduce the frequency of relapse and bring many risks associated with the effect on healthy cells of the body. The purpose of developing targeted therapy, including Flt3 kinase inhibitors, is to prevent this adverse effect of chemotherapeutics. The aim of the research carried out as part of this diploma thesis was to determine the effect of the newly synthesized Flt3 inhibitor K1872 on the proliferation of leukemic cells with wild type Flt3 kinase (THP-1) and cells with the most frequently occurring Flt3-ITD mutation (MOLM-13 and MV-4-11). The effects of the inhibitor on cell proliferation, induction of apoptosis and changes in protein expression of selected signaling pathways were investigated using the methods described below. The results of the individual experiments demonstrated a significant effect on the reduction of the proliferation of leukemic cells with Flt3-ITD mutation (MOLM-13 and MV-4-11) and when compared with the results of the preclinical evaluation of midostaurin, an inhibitor used in clinical practice, they show the same trend.