ABSTRACT

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Acute myeloid leukemia (AML) represents an aggressive hematological malignant disease. Despite the advanced therapeutic approaches, it has a very low curability and poor treatment response with 5-year overall survival under 30%. The heterogeneity and interindividual variability of the disease is explained by the identification of numerous cytogenetic and molecular aberrations. The aberration of FMS-like tyrosine kinase receptor 3 (FLT3), which occurs at almost one third of AML patients, is the most important for patient prognosis. Physiologically, FLT3 is expressed by early myeloid and lymphoid progenitor cells, and it regulates the proliferation and differentiation of hematopoietic cells. There are two major mutations of FLT3 called internal tandem duplication (ITD) and tyrosine kinase domain mutation (TKD). Both types lead to constitutive activation of FLT3 receptor which results in unlimited proliferation and decreased cell apoptosis. Midostaurin, a multi-kinase inhibitor, proved a significant benefit in treating patients with FLT3 mutation. After this success, other compounds targeting FLT3 have been introduced and clinically tested. Based on the structure of our lead compound K1872, we have developed 10 novel candidates for the treatment of AML. Newly synthesized compounds were tested *in vitro*, specifically, the antiproliferative and proapoptotic effect in selective leukemia cell lines. We will also establish antiproliferative activity against AML patient-derived primary mononuclear cells distinguishing FLT3 mutation status.