Evaluation of New FLT3 Inhibitors as New Drugs in Acute Myeloid Leukemia

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Mutations in the FLT3 receptor, present in approximately one third of patients with acute myeloid leukemia (AML), are associated with an aggressive course of the disease, a high risk of relapse, and a low survival rate. Although FLT3 inhibitors represent a major advance in the targeted therapy of AML, the development of resistance significantly limits their long-term efficacy and remains one of the main causes of therapy failure. This work aimed to characterize three newly synthesized compounds, firstly to evaluate their effect on the proliferation of AML cell lines, and to assess their specific effect on cells with a mutated FLT3 receptor. The second aim was to determine the effect of these compounds on a gilteritinib-resistant cell line. Using an in vitro colorimetric MTT assay, the cytostatic/cytotoxic effects of the tested compounds were evaluated in comparison with the clinically used inhibitors midostaurin and quizartinib. While the new agents showed lower efficacy than the established inhibitors in the FLT3 mutated lines MV4-11 and MOLM-13, they achieved the lowest resistance factor values ??in the gilteritinib-resistant line MV4-11 g45. The obtained results provide an important basis for the further development of novel FLT3 inhibitors with more favorable properties, which could represent an alternative in the treatment of AML, including forms resistant to conventional FLT3 inhibitors, and contribute to expanding therapeutic options for patients with AML that are still difficult to treat.

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