Specific Features of the FLT3+ Acute Myeloid Leukemia Course

Asiyat M. Radzhabova MD, Ekaterina V. Motyko PhD, Lubov B. Polushkina PhD, Marina P. Bakay PhD, Anastasiya A. Kuzyaeva MD, Nadezhda Potihonova PhD, Irina S. Martynkevich PhD, Sergey V. Voloshin PhD
Russian Research Institute of Hematology and Transfusiology, Saint-Petersburg, Russian Federation

Context

Preliminary stratification into prognostic risk groups is a mandatory component of the AML patient's treatment, which allows for optimizing the intensity of chemotherapy (CT), as well as planning and justifying allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Objective

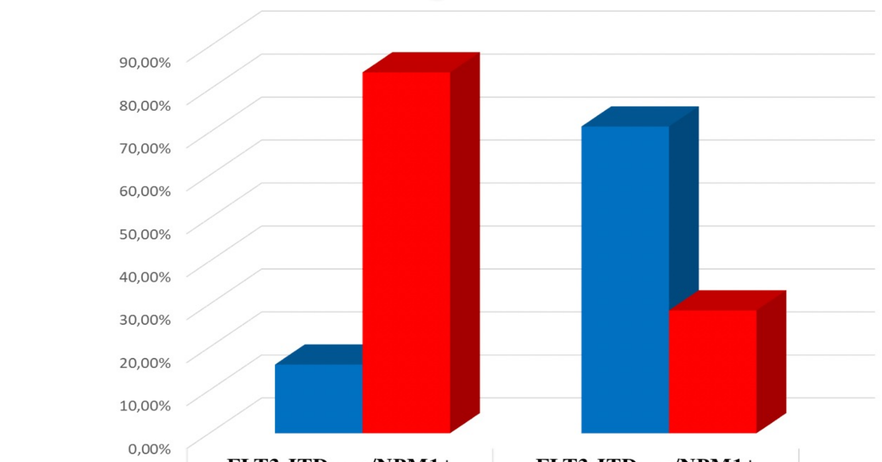
To evaluate the effects of the FLT3 gene mutational status and the allele burden (AB) magnitude in FLT3-ITD patients on the course of AML.

Patients or Other Participants

Study of the FLT3 gene mutational status effect on the course of the disease in 280 patients was carried out. The dynamics of the magnitude of the AB in the FLT3-ITD cases were analyzed in the context of CT, allo-HSCT, and the impact of the AB on survival rates in 91 patients.

Summary

In the study group, the frequency of FLT3 accounted for 30.5% (FLT3-ITD-24% (48/199), the frequency of FLT3-TKD was 5.5% (11/199), the combination of FLT3-ITD and FLT3-TKD was found in 1.0% (2/199)); the rest of the patients, 69.5% (138/199), had no mutations in the FLT3 gene. Mutations in NPM1 gene were detected significantly more frequently in the FLT3-ITD–in 37 (32.4%) out of 114 patients (p=0.0001). Two groups were identified according to the magnitude of AB in the FLT3-ITD mutations: low AB (<0.5)-n=50 (55%) and high AB (≥0.5)-n=41 (45%). Patients with high AB FLT3 gene, compared with low AB, had a high level of leukocytes (p<0.001) and bone marrow blast cells (p=0.04). Patients FLT3-ITDlow/NPM1+ achieved CR (complete clinical and hematological remission) more often compared with FLT3-ITDhigh/NPM1+, with CR rate of 71.4% and 16.0%, respectively ($\chi 2$=11.2; p=0.04). The efficacy of allo-HSCT in FLT3+ was significantly higher only in terms of OS; it was not achieved in the allo-HSCT(+) (n=24), compared with the median of 8 months recorded in the allo-HSCT(-) (n=119)(p<0.00001). The application of CT reduced AB by 1.5 (p<0.001). Sequential use of CT and allo-HSCT showed higher efficacy (p<0.001).



	FLT3-ITDвыс/NPM1+	FLT3-ITDниз/NPM1+
Remission	16,00%	71,40%
No remission	84,00%	28,60%

The frequency of complete remission depending on the mutational achievement of the FLT3 and NPM1 genes

Discussion

AML patients with mutations in the FLT3 gene require an individualized approach with inclusion of targeted drugs into the scheme of treatment, which allows survival rates to improve.