THE ADDITION OF FLT3 INHIBITOR TO STANDARD INDUCTION CHEMOTHERAPY INCREASES THE RATES OF COMPLETE REMISSIONS IN FLT3-MUTATED ACUTE MYELOID LEUKEMIA

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Introduction: Fms-like tyrosine kinase-3 (FLT3) gene mutations are most frequent molecular abnormalities in acute myeloid leukemia (AML) and internal tandem duplications (ITD) in the juxtamembrane domain occur in ~25% of newly diagnosed cases. The addition of inhibitors of FLT3 to standard induction chemotherapy (IC) is a promising strategy to overcome the historically poor prognosis of FLT3-mutated AML. Here, we evaluate the impact on remission status of the addition of Sorafenib to IC in de novo AML patients, fit for intensive therapy.

Material and methods: This is a retrospective study including 25 previously untreated patients with FLT3-mutated AML. FLT-ITD mutation was detected by fluorescent polymerase chain reaction (PCR) and capillary electrophoresis of PCR products by automatic DNA analyzer at diagnosis and after induction chemotherapy. Patients received frontline Daunorubicin- Cytarabine (DA) "3+7" regimen. Sorafenib was administered at a dose of 400mg daily for 14 days from day +1 on.

Results: The mean age of study population was 60 years (range: 16-74). 14 patients received DA without targeted drug. Only four of them achieved complete remission (CR). Interestingly, all of them had additional nucleophosmin 1 (NPM1) mutation, hence they are stratified into the intermediate risk group. In contrast, among 11 patients receiving Sorafenib, 9 patients achieved CR and all of them were minimal residual disease (MRD) negative at the end of two induction cycles. In addition, 6 of them had FLT3 as sole mutation.

Conclusion: Sorafenib in combination with DA 3+7 is a highly effective treatment regimen, resulting in higher rates of post-induction complete remissions in FLT3+ AML.