AMLGlobalPortal

FLT3

Does FLT3-ITD mutation have an impact on prognosis of APL patients?

 **Anna Bartus**  **Cynthia Umukoro** | Feb 12, 2018

Progress in the treatment of Acute Promyelocytic Leukemia (APL) has changed course from a highly fatal to a highly curable disease with the use of novel drugs such as all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). The current risk stratification system has also led to dramatic improvement in managing the disease: nowadays, treatment regimens are different for low and high-risk groups.[1] However, the clinical impact of *Fms Like Tyrosine 3 Internal Tandem Duplication* (*FLT3-ITD*) mutations remain controversial. In a recent issue of Hematology, Yingchao Fan *et al.* from Shidong Hospital, Shanghai, China, published results from their meta-analysis (MA) which investigated the clinical significance of *FLT3-ITD* mutation in patients with APL.

Using multiple online databases for the systematic review element of the MA, the authors identified 17 trials comprising of 2,252 APL patients. The identified studies used in this review focused on the relationship between *FLT3-ITD* and the Complete Remission (CR) rate, the 5-year Disease Free Survival (DFS) rate or the 5-year Overall Survival (OS) rate of adult APL. The treatment regimens in the identified 17 studies were comparable. All patients received standard chemotherapy, only the type of chemotherapy was somewhat different in each study. Patients were divided into two groups based on their mutational status; *FLT3-ITD*-positive group and *FLT3-ITD*-negative (*FLT3-ITD-WT*) group.

Key findings of the meta-analysis:

- CR rate in evaluable APL patients (n = 1,875) from 13 studies:
  - CR rate in the *FLT3-ITD* -positive group was inferior compared to the $FLT3\text{-}ITD^{WT}$ group; Odds Ratio (OR) = 0.53 (95% CI, 0.30 – 0.95), $P = 0.03$
- 5-year OS rate in evaluable APL patients (n = 2,252) from all 17 studies:
  - Compared to patients in the $FLT3\text{-}ITD^{WT}$ group, OS was significantly lower in *FLT3-ITD* - positive patients; OR = 0.47 (95% CI, 0.29 – 0.75), $P = 0.002$
- 5-year DFS rate in evaluable APL patients (n = 1,931) from 15 studies:
  - DFS in the *FLT3-ITD*-positive cohort was significantly poorer than $FLT3\text{-}ITD^{WT}$ patients; OR = 0.48 (95% CI, 0.29 – 0.78), $P = 0.003$

In conclusion, based on CR rate after induction therapy, 5-year OS, and 5-year DFS, the authors stated that *FLT3-ITD* positivity was likely to indicate poor prognosis in patients with APL.

Why did some other studies have a different conclusion? The authors added that “perhaps the treatment protocols affected the results. Although the treatment principle in all the trials was the same, drugs such as ATO added to induction therapy might improve survival”. They further added that the number of patients in this meta-analysis might not be

sufficient enough and thus other on-going studies might lead to a change in the findings of this study.

References

1. Cicconi G.L., Lo-Coco F. Current management of newly diagnosed acute promyelocytic leukemia. Annals of Oncology. 2016 Aug 1. DOI: 10.1093/annonc/mdw171.
2. Fan Y. et al. The clinical significance of FLT3 ITD mutation on the prognosis of adult acute promyelocytic leukemia. Hematology. 2018 Dec 18. DOI: 10.1080/10245332.2017.1415717. [Epub ahead of print].