LETTER to the EDITOR

Survival Outcome of AML Patients with and without TKD Mutations

Asian Pac J Cancer Prev, **15 (24)**, 10995

Dear Editor

Acute myeloid leukaemia (AML) is a disease of heterogenic nature (Su et al., 2013; Ahmad et al., 2014). "Almost one third of AML patients have normal karyotype and fall in a standard risk group" (Kotaridis et al., 2001; Karabacak et al 2010). Significant proportion of AML cases have normal karyotype and characterized by the presence of prognostic markers such as FLT3-ITD,(internal tandem duplication) and TKD (point mutation), NPM1 and CEBPA (Ishfaq et al., 20012; Renneville et al., 2014).

Tyrosine kinase mutations induce "constitutive tyrosine phosphorylation, enhance cell proliferation and development of hematologic malignancies" (Liang et al., 2003). The clinical and prognostic relevance of the TKD mutations is less clear (Liang et al., 2003) and are more dependent on other mutations as reported by various authors (Thieda et al., 2002). More generally FLT3-TKD mutations is less frequent (7%) than internal tandem duplications (20-25%) (Weisberg et al, 2010). Although, there is "considerable heterogeneity" amongst subtypes. The frequency of FLT3-TKD mutations is not equal in all AML subtypes.

The association of FLT3-TKD mutations with outcome is controversial and more difficult to study because of low number of cases (Mead et al, 2008). In order to investigate the role of TKD mutation in TKD positive and TKD negative patient and their effect on overall survival we have examined small cohort of 31 patients. We performed Polymerase chain reaction and gell electrophorhesis (Thiede et al., 2003). The data was analysed with SPSS version20. We have not compared any other haematological parameters, regarding this study, except the overall survival in AML patients on the basis of presence and absence of FLT3-TKD mutation. Independent samples t-test was performed at 0.05 significance level. In statistical test, p-value (0.492>0.05) resulted in insignificant difference between the overall survival of AML patients with and without TKD mutation. Although TKD mutations have controversial outcome generally but there was no significant difference found in overall survival of TKD positive and TKD negative patients in this study.

References

Ahmad F, Mohota R, Sanap S, Mandava S, Das BR (2014). Molecular evaluation of DNMT3A and IDH1/2 gene mutation: frequency, distribution pattern and associations with additional molecular markers in normal karyotype indian acute myeloid leukemia patients. *Asian Pac J Cancer Prev*, **15**, 1247-53

D-C Liang1, L-Y Shih2, I-J Hung (2003). FLT3-TKD mutation in childhood acute myeloid leukemia. *Leukemia*, **17**, 883-6

Ishfaq M, Malik A, Faiz M, et al (2012). Molecular characterization of FLT3 mutations in acute leukemia patients. *Asian Pac J Cancer Prev*, **13**, 4581-85

Kottaridis PD, Gale RE, Frew ME, et al (2001). The presence of a FLT3 internal tandem duplication in patients with acute myeloid leukemia (AML) adds important prognostic information to cytogenetic risk group and response to the first cycle of chemotherapy: analysis of 854 patients from the United Kingdom Medical Research Council AML 10 and 12 trials. *Blood*, **98**, 1752-9.

Karabacak, BH, Erbey F, Bayram I, et al (2010). Fms-like tyrosine kinase 3 mutations in childhood acute leukemias and their association with prognosis. *Asian Pac J Cancer Prev*, **11**, 923-7.

Mead AJ, Gale RE, Hills RK, et al (2008) Conflicting data on the prognostic significance of FLT3/TKD mutations in acute myeloid leukemia might be related to the incidence of biallelic disease. *Blood*, **112**, 444-5.

Renneville A, Abdelali RB, Chevret S, et al (2014). Clinical impact of gene mutations and lesions detected by SNP-array karyotyping in acute myeloid leukemia patients in the context of gemtuzumab ozogamicin treatment: Results of the ALFA-0701 trial. *Oncotarget*, **5**, 916-32.

Shahab S, Shamsi T, Ahmed N (2012). Molecular Involvement and Prognostic Importance of Fms-like Tyrosine Kinase 3 in Acute Myeloid Leukemia. *Asian Pac J Cancer Prev*, **13**, 4215-20.

Su L, Gao SJ, Tan YH, Han W, Li W (2013). Associations Between Age, Cytogenetics, FLT3-ITD, and Marrow Leukemia Cells Identified by Flow Cytometry. *Asian Pac J Cancer Prev*, **14**, 5341-4.

Thiede C, Steudel C, Mohr B, et al (2002). Analysis of FLT3-activating mutations in 979 patients with acute myelogenous leukemia association with FAB subtypes and identification of subgroups with poor prognosis. *Blood*, **99**, 4326-35

Weisberg E, Sattler M, Ray A, Griffin JD (2010) Drug resistance in mutant FLT3-positive AML. *Oncogene*, **29**, 5120-34.

Sadaf Shahab[1]*, Khaleeq un Nisa[1], Muhammad Nadeem[2], Danish Zahid[1], Saqib Ansari[2], Tasneem Farzana[2], Mehwesh Taj[2], Munira Borhany[2], Nuzhat Ahmed[1,2], Tahir S Shamsi[2]

[1]Department of Molecular Genetics, [2]Department of Hematology, NIBD Postgraduate Institute of Life Sciences Karachi, Pakistan
**For correspondence: sadaf_shahab99@yahoo.com*