

LETTER to the EDITOR

Outcome of Inversion 16 in TKD Positive and Negative Acute Myeloid Leukemia Patients

Asian Pac J Cancer Prev, 17 (4), 2343-2344

Dear Editor

A “considerable number” of acute myeloid leukemia (AML) cases have normal karyotype and “express prognostic markers” such as FLT3-ITD,(internal tandem duplication) and TKD (point mutation), NPM1 and CEBPA (Ishfaq et al., 2012; Ahmad et al., 2014; Renneville et al., 2014). Although, great versatility observed amongst subtypes. The frequency of FLT3-TKD mutations is not equal in all AML subtypes. It showed “preferential occurrence” in the intermediate cytogenetic subgroup in PML-RARA and inv(16) AML (Mead et al., 2007; Li et al., 2012). Various authors reported that TKD mutations are more frequent in inversion 16 groups (Kock 2012). In order to investigate any possible association between TKD mutation and inversion 16 we have analysed 35 adult AML patients for TKD point mutation as described elce

where (Thiede et al., 2002). Briefly genomic DNA was extracted and PCR amplification was performed in a 50 µl reaction buffer. PCR products were digested for 1 hour at 37°C and analysed by 2% agarose gel electrophoresis (Thieda et al., 2002).

The frequency of TKD in different studies varies in general. Some studies reported its incidence 5.8% to 7.7% in AML while some reported its incidence from 8 to 12% (Table 1). Our FLT3-TKD D835mutation is 14.2% which is very close to the study done by Frohling et al. There are very few studies which analyse the association of TKD with inversion 16. The association of FLT3-TKD mutations with the over all survival is controversial and more difficult to study because of low number of cases (Mead et al., 2007). In order to get more conclusive picture we also examined some important studies which at least comprises of 95 samples (Table 1).

We have examined a small cohort of 35 patients. In order to investigate the role of TKD mutation in over all survival and their association with inv 16, we only investigate those cases who are negative for ITD which is reported as a bad prognostic marker by several authors. Although we have examined a small cohort of patients but we have found strong association between TKD mutation and inversion 16. We just found 1 case of inversion 16 out of 5 TKD mutant cases which is a very high frequency and comparatively this patient showed the over all better survival. We also compared various haematological parameters in TKD positive and TKD negative patients

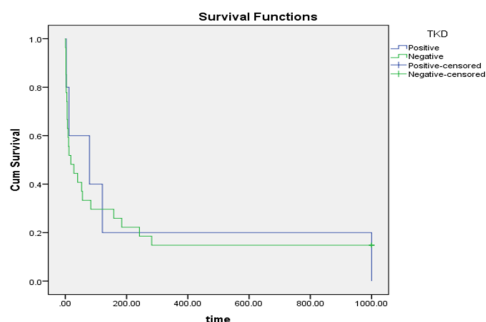


Figure 1. Survival Analysis

Table 1. TKD Mutations with and without Inversion 16

TKD D835 mutation(%)	No of cases with inversion 16	References
4/97(4.1%)	No inversion 16 mentioned	Elyamy etal 2014
3/91(3.9%)	No inversion 16 mentioned	Liang et al 2003
147/3082(4.7%)	Out of 119 inv 16 cases only 6 have TKD mutation	Bacher et al 2007
7/97(7.2%)	No inversion 16 mentioned	Abu Duhier et al 2001
30/429(7.0%)	No inversion 16 mentioned	Yamamoto et al 2001
75/979(7.7)	No inversion 16 mentioned	Thiede et al 2002
16/208(7.6%)	No inversion 16 mentioned	Moreno et al
56/1053(13.3%)	Out of 420 inv 16 cases only 56 have TKD mutation	Kok et al
25/175(14%)	17% of the patients had FLT# mutation with a 3 fold higher frequency of TKD compared with ITD**	Paschka et al 2013
3/110(2.5%)	No inversion 16 mentioned	Murphy etal
4/113(3.5%)	1/4 has inv 16	Colovic et al 2007
68/617(11%)	No inversion 16 mentioned	Schlenk et al 2008
19/120(15.8%)	No inversion 16 mentioned	Shih et al 2004
11/120(8.5%)	No inversion 16 mentioned	Gari et al 2008
37/672(5.5%)	4/11 has inv 16	Janke et al 2014
32/224(14%)	No inversion 16 mentioned	Frohling et al

**+This study mainly done on group of inv(16) patients

Table 2. Test of Equality of Survival Distributions for the Different Levels of TKD

	Overall Comparisons		
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	0.001	1	0.981

Table 3. Independent Samples Test For Variable Parameters

	Independent Samples Test					
	Levene's Test for Equality of Variances		t-test for Equality of Means			
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference
Age	1.968	.170	.367	32	.716	3.15
Hb Level	.070	.793	-1.809	30	.080	-1.95
TLC	.153	.698	.630	30	.534	20.08
Blast	.097	.759	.546	25	.590	6.61
Platelets	1.339	.256	-.774	30	.445	-28.21

(Table 3) but we have not found any significant difference between these two groups. In conclusion there is a “preferential occurrence” of inversion 16 and better over all survival with TKD mutant sub types but low sample size is a limitation in this study.

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