Complex or monosomal karyotype and not blast percentage is associated with poor survival in acute myeloid leukemia and myelodysplastic syndrome patients with inv(3)(q21q26.2)/t(3;3)(q21;q26.2): a Bone Marrow Pathology Group study

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Running heads:

Poor survival in inv(3)/t(3;3) AML and MDS

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Supplementary Methods

Categorical variables were summarized using frequencies and percentages, while continuous variables were summarized using medians, minimum and maximum values. The relationship between AML and MDS and categorical variables was described using Chi-square test or Fisher's Exact test. The relationship between AML and MDS and continuous variables was described using t-test. All *P* values were two-tailed, and $P<0.05$ was considered significant. Kaplan-Meier method was used for univariable survival estimates (Logrank test), and a univariable Cox proportional hazards (PH) regression model was used to generate hazard ratios (HR) and 95% confidence intervals (CI). Overall survival (OS) was calculated from the time of initial demonstration of inv(3)/t(3;3). HR is provided for the continuous measures based on univariable Cox PH models. Factors with $P<0.05$ in univariable model were considered for the multivariable Cox PH model. User defined contrasts were used to analyze the pairwise differences between therapy types. Signed rank test was used for comparison of categories in IPSS and IPSS-R systems. Analyses were done using SAS software (version 9.1; Cary, NC) and MedCalc software (version 12.1.4.0; Ostend, Belgium).

Supplementary Table 1. Types of therapies received by MDS and AML with inv(3)/t(3;3) patients

Treatment Modalities	MDS with inv(3)/t(3;3) (N=40)	AML with inv(3)/t(3;3) (N=63)	MDS and AML with inv(3)/t(3;3) (N=103)
Chemotherapy with Stem Cell Transplant	8	18	26
Chemotherapy Alone	17	34	51
High Intensity Chemotherapy	5	26	31
Low Intensity Chemotherapy	8	3	11
Unspecified	4	5	9
Supportive Therapy	12	10	22
Unknown Therapy	3	1	4

High intensity chemotherapy; 7 + 3 (cytarabine + anthracycline based regimen [daunorubicin, idarubicin, mitoxantrone]), etoposide, total body irradiation, high dose intermittent cytarabine (HiDAC), clofarabine, antisoma, FLAG (fludarabine, high dose cytarabine, G-CSF), arsenic/mylotarg, busulfan

Low Intensity Chemotherapy; 5-azacitidine, decitabine, capacitibine, lenalidomide, sirolimus, thalidomide, antithymocyte globulin, low dose cytarabine, triapine plus fludarabine, cis-retinoic acid, interferon, rituximab, imatinib

Supportive; transfusions, hydroxyruea, erythropoiesis or granulocyte/ granulocyte-macrophage stimulating factors, cyclosporine, no treatment

(Abbreviations: MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; inv(3)/t(3;3): inv(3)(q21q26.2)/t(3;3)(q21;q26.2); N: number)

Supplementary Table 2. Comparison of clinical and pathologic features in inv(3)/t(3;3) MDS patients with and without transformation to AML.

	MDS with transformation to AML	MDS without transformation to AML	*P* value
N	20	17	
Age (years)	61.5	67.5	0.07
Sex (M/F)	9/11	8/9	0.97
WBC (x 10^9/L)	2.5	3.6	0.24
ANC (x 10^9/L)	0.68	1.16	0.48
Hb (g/dL)	9.4	9.0	0.91
Platelet (x 10^9/L)	114.0	91.0	0.78
Hepatosplenomegaly %	33.3	6.6	0.20
Clinical outcome (expired; %)	17 (85.0%)	10 (58.8%)	0.44
Median follow-up (mo)	13.0 (5-37)	5.7 (1-78)	0.48
Therapy CTX CTX-T Supportive	 11 (58.0%) 4 (21.0%) 4 (21.0%)	 4 (26.7%) 4 (26.7%) 7 (46.6%)	0.16
Karyotype Structurally complex Non-complex	 3 (15.0%) 17 (85.0%)	 3 (17.6%) 14 (82.4%)	0.88
Karyotype Monosomal Non-monosomal	 4 (20.0%) 16 (80.0%)	 0 (0.0%) 17 (100%)	0.31
BM Blast %	6	4	0.12
BM Cellularity %	40	35	0.94
Dysmegakaryopoiesis	20 (100%)	17 (100%)	0.73
Dyserythropoiesis	16 (80%)	14 (82.3%)	0.31
Dysgranulopoiesis	16 (80%)	17 (70.5%)	0.23

Data: Median (range)
(Abbreivationa: inv(3)/t(3;3): inv(3)(q21q26.2)/t(3;3)(q21;q26.2); MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; N: number; WBC: white blood cell; ANC: absolute neutrophil counts; Hb: hemoglobin; mo: months; CTX; chemotherapy, CTX-T: chemotherapy with stem cell transplant; BM: bone marrow)