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## Prognostic Significance of 11q23 Aberrations in Adult Acute Myeloid Leukemia and the Role of Allogeneic Stem Cell Transplantation

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### Abstract

The clinical features and outcomes of 148 patients with acute myeloid leukemia (AML) and 11q23 chromosomal abnormalities were compared with those of 2640 patients with non-11q23 AML. Patients with t(9;11), t(6;11), or other 11q23 balanced translocations [t(11;v)(q23;v)] presented at a younger age and with higher percentage of bone marrow blasts. Unbalanced 11q23 abnormalities were commonly associated with deletions of chromosomes 5q, 7q and/or complex karyotypes. In multivariate analysis, when compared to patients with non-11q23 AML and unfavorable risk karyotype, there was a significant difference in overall survival (OS) for patients with t(9;11) ( $P = .004$ ), whereas there were no difference in OS for patients with t(6;11) ( $P = .62$ ), t(11;19) ( $P = 0.20$ ), and unbalanced 11q23 aberrations ( $P = .85$ ) or t(11;v)(q23;v) ( $P = 0.59$ ), indicating that t(9;11) has an independent intermediate prognostic factor, with all others poor prognostic factors for OS; this was further confirmed by comparing them with patients with non-11q23 AML and intermediate risk karyotype. Using intention-to treat analysis based on donor availability, we also noted that allogeneic stem cell transplant (SCT) in first remission had a significant benefit towards improving OS ( $P < 0.001$ ) and relapse-free survival ( $P < 0.001$ ) in patients with AML and 11q23 abnormalities.

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## Keywords

AML; 11q23 cytogenetic abnormalities; complete remission; prognosis allogeneic stem cell transplantation

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## INTRODUCTION

Cytogenetic abnormalities in leukemia cells are strongly associated with distinct clinical subgroups and are predictive of both clinical features and therapeutic outcome.<sup>1–4</sup> Recurrent cytogenetic abnormalities in chromosome 11q23 involving the mixed-lineage leukemia (*MLL*) gene have been observed in 3%–4% of adult patients with acute myeloid leukemia (AML), in 3%–7% of adults with acute lymphoblastic leukemia,<sup>5</sup> and at even higher rate in infant leukemia.<sup>6, 7</sup> To date, more than 60 translocation partner genes of 11q23 have been identified.<sup>8</sup>

*MLL* encodes a histone methyltransferase that is critical for maintaining gene expression during embryonic development and hematopoiesis. *MLL* gene translocations generate chimeric *MLL* fusion proteins that directly bind to DNA and positively regulate gene transcription. These events result in aberrant expression of downstream *MLL* targets, including the *HOX* gene, thereby leading to leukemic transformation.<sup>8, 9</sup> Recent studies have shown that the prognosis of 11q23/*MLL* AML is heterogeneous depending upon the 11q23 fusion partner.<sup>10, 11</sup> In addition, the prognosis of AML with 11q23 abnormalities with the same translocation partner differs between adults and children.<sup>10–13</sup> As a result, in the 2008 edition of the World Health Organization (WHO) classification of myeloid neoplasms, the category of AML with 11q23/*MLL* abnormalities was revised to focus on AML with t(9;11)(p22;q23)/*MLLT3-MLL*, with the notation that rearrangements of *MLL* with other fusion partners need to be specified upon AML diagnosis.<sup>14</sup>

Because adult AML cases with 11q23 abnormalities are rare, the clinical features and prognostic significance of the abnormalities other than t(9;11) are not well known. To our knowledge, the prognostic significance of unbalanced 11q23 aberrations has not been reported to date. The prognostic impact of additional chromosomal abnormalities in patients with 11q23 aberrations is also not clear. The existing information about this subgroup is based on data from only a few clinical trials with potential for selection bias. Furthermore, information on the potential therapeutic role of allogeneic stem cell transplantation (allo-SCT) in this subgroup is scarce, as most of the published studies involved groups that were too small to allow definitive conclusions.<sup>15, 16</sup>

In the present study, to characterize their clinical features, assess their outcomes in response to therapy, and evaluate the significance of allo-SCT performed at first complete remission (CR1), we retrospectively analyzed the data from 148 adult patients with newly diagnosed 11q23 AML between January 1990 and February 2011 who were treated at our institution. We clearly demonstrate that t(6;11), t(11;19), unbalanced 11q23 aberrations and t(11;v)(q23;v) are independent poor prognostic factors whereas patients with t(9;11) have intermediate risk disease. We also demonstrate that allo-SCT in CR1 has a significant

benefit for improving overall and relapse-free survival for patients with AML and 11q23 abnormalities.

## PATIENTS AND METHODS

### Patients

We searched the database of the department of leukemia at the University of Texas – MD Anderson Cancer Center. Between January 1990 and February 2011, 2788 consecutive patients with newly diagnosed AML with available cytogenetic analysis were identified and were the subject of this study [excluding patients with acute promyelocytic leukemia, and those with core binding factor leukemia with t(16;16)/inv(16) or t(8;21)]. Upon initial diagnosis, 148 of the 2788 patients had 11q23 abnormalities detected by conventional cytogenetic analysis; these were confirmed by fluorescence in situ hybridization analysis in 29 patients. AML with MLL partial tandem duplications was not included in this study as it is considered as a distinct entity.<sup>14</sup> The remaining 2640 patients were defined as having non-11q23 AML. Among the patients with 11q23 AML, 144 (97%) underwent chemotherapy regimens consisting of high-dose ara-C (HDAC, 1 g/m<sup>2</sup> per dose) alone (n=3) or plus idarubicin (n=85), plus fludarabine (n=20), or plus other agents such as clofarabine, topotecan, troxacitabine, or liposomal daunorubicin (n=20); non-HDAC (<1 g/m<sup>2</sup> per dose) plus daunorubicin or clofarabine (n=9); 7 patients had other non-ara-C based regimens. Among the 2640 non-11q23 reference group, 131 patients received supportive treatment only (5%). 1838 patients received HDAC based regimens (70%), 297 patients received non-HDAC based regimens (11%), and 374 patients received other non-ara-C based regimens (14%). All patients were treated on prevailing clinical trials and gave written informed consent to participate. The current study was further approved by the Institutional Review Board at The University of Texas MD Anderson Cancer Center.

### Subgroups of 11q23 abnormalities

11q23 abnormalities were classified into five groups. Group A) t(9;11) (n=65; 44%) included t(9;11)(p22;q23) (n=58) and t(9;11)(p21;q23). Group B) t(6;11) (n=12; 8%) included t(6;11)(q27;q23). Group C) t(11;19) (n=18; 12%) included 12 cases with t(11;19)(q23;p13), 3 with t(11;19)(q23;p13.3), 2 with t(11;19)(q23;p13.1) and one with t(11q23;p13.2). Group D) unbalanced 11q23 aberrations (n=41; 28%) included del(11)(q23) (n=32) and add(11)(q23), inv 11q23, or dic 11q23 (n=9;). Group E) t(11;v)(q23;v) (n=12; 8%) comprised of other balanced 11q23 translocations, including two patients each with t(10;11) and t(11;17), and one each with t(11;15), t(7;11), t(X;11), dic(11;12), t(3;11), t(11;22), t(4;11), and t(11;11). These distributions are similar to those reported in previous studies,<sup>17, 18</sup> with the exception of a relatively lower frequency of t(10;11). Additionally, the frequency of unbalanced 11q23 aberrations was relatively higher in our study. Cases of non-11q23 AML were grouped into two cytogenetic risk categories (intermediate and unfavorable) according to the European Leukemia Net criteria.<sup>1</sup> The outcomes and clinical features of the cases in the five 11q23 AML subgroups were compared with those of the non-11q23 AML cases.

## Statistical analysis and definitions

Complete remission (CR), overall survival (OS), event-free survival (EFS), and relapse-free survival (RFS) were defined on the basis of criteria recommended by the International Working Group.<sup>19</sup> A Wilcoxon rank-sum test was used to make pair wise comparisons of continuous variables between cytogenetic subgroups, and a Kruskal-Wallis test was used to compare continuous variables among more than two subgroups. Categorical variables were compared using Fisher's exact test. The Bonferroni method was used to adjust the type I error when multiple comparisons were used. The Kaplan-Meier method was used to estimate the time-to-event variables. Log rank tests were conducted to compare the survival among the various cytogenetic subgroups. Cox proportional hazards models were used to evaluate the ability of the covariates to predict the time-to-event variables. For each fitted Cox regression model, non-significant variables in univariate analyses were eliminated in a step-down fashion using a *P* value cutoff of *P* = 0.05. All computations were carried out using SAS software version 9.1 and S-Plus software version 8.04.

## RESULTS

### Incidence and clinical characteristics of 11q23 AML

The frequency of 11q23 AML within intermediate and unfavorable cytogenetic risk AML was 5.3% (148/2788). Among the 2640 patients with non-11q23 AML, 1679 had intermediate-risk cytogenetics, and 961 had unfavorable-risk cytogenetics. Among the 148 patients with 11q23 AML, 78(52%) had de novo AML, and 58(40%) had therapy-related AML (t-AML); in 12 (8%) patients the disease was secondary to a prior myelodysplastic syndrome or myeloproliferative neoplasm (s-AML).

The median age of patients with 11q23 AML was 54 years (range, 17 to 84 years), and 61 (41%) patients were male. Of note, 60 of 148 (41%) cases were classified as the French-American-British (FAB) classification M5 (FAB-M5), and 32 (22%) were classified as M4 (FAB-M4). The presenting features of various 11q23/MLL AML subgroups are shown in Table 1. Patients with t(9;11), t(6;11), and t(11;v)(q23;v) presented at a younger age ( $P < 0.001$ , = 0.002 and  $< 0.001$ , respectively) and had a higher percentage of bone marrow blasts ( $P < 0.001$ ,  $< 0.001$  and = 0.04, respectively) at diagnosis than those in the non-11q23 reference group. Proportion of patients with FAB-M5 was higher among patients with all 11q23 AML subgroups than in the reference group ( $P < 0.001$ ). Patients with t(9;11) were more likely to be female (69%) than the non-11q23 reference group (41%;  $P < 0.001$ ). Patients with t(9;11) were more likely to have t-AML and/or s-AML compared to those with non-11q23 AML ( $P = 0.008$ ),<sup>20</sup> whereas patient with t(6;11) commonly presented with de novo AML ( $P = 0.007$ ). No differences in white blood cell counts, platelet counts, hemoglobin levels, FAB-M4 incidence, t-AML or s-AML incidence were observed between the 11q23 subgroups and the non-11q23 reference group (Table 1).

### Del (5q)-/5, del (7q)-/7, complex karyotypes, and additional trisomy 8 with 11q23 abnormalities

The incidence of additional cytogenetic abnormalities including del5/5q-, del7/7q-, and/or complex karyotypes was significantly higher in patients with unbalanced 11q23 aberrations

than in the non-11q23 reference group ( $P < 0.001$ ), whereas the incidence of these additional abnormalities was significantly lower in patients with t(9;11) ( $P = 0.008$ ) and t(11;19) ( $P = 0.006$ ) than in the non-11q23 reference group. The incidence of additional trisomy 8 was higher in patients with t(9;11) and unbalanced 11q23 aberrations than in the non-11q23 reference group ( $P = 0.003$  and  $0.02$ , respectively).

### Treatment response and clinical outcome

The median follow-up time in all patients ( $n = 2788$ ) was 5 years. The overall CR rate for the 144 patients with 11q23 aberrations who received induction chemotherapy was 68% ( $n = 98$ ); The median OS time in the 11q23 AML group and the non-11q23 AML reference group was 8.5 months (95% confidence interval, 6.4 to 11.9 months) and 9.5 months (95% confidence interval, 9.0 to 10.2 months), respectively ( $P = 0.32$ ; data not shown). Patients with t(9;11) had OS and EFS similar to intermediate non-11q23 reference group, where as all other 11q23 groups (data not shown) had OS and EFS comparable to unfavorable non-11q23 reference group (Figure 1)

The 5-year OS rates and EFS rates were shown in Table 1. The OS rate was lower in patients who had 11q23 AML with del(5q)-5, del(7q)-7, and/or complex karyotypes than in those without del(5q)-5, del(7q)-7, and/or complex karyotypes ( $P < .001$ ; Figure 2). There was no significant difference in OS rates between patients who had 11q23 AML with additional trisomy 8 and those without additional trisomy 8 ( $P = 0.96$ , data not shown).

### Risk factor analysis

To determine the prognostic impact of each 11q23 subgroup, we used Cox regression models when age, sex, race, white blood cell counts, platelet counts, hemoglobin levels, lactate dehydrogenase, percentage of bone marrow blasts, type of AML (de novo vs. t-AML/S-AML), type of treatment, performance status, and the five 11q23 subgroups were considered. Cytogenetic abnormalities were excluded because of overlap with five 11q23 subgroups. Multivariate analysis revealed that only t(9;11) was an independent intermediate risk factor for OS when compared to patients with unfavorable non-11q23 AML (hazard ratio [HR] = 0.61;  $P = 0.004$ ). There was no significant difference in OS when patients with intermediate non-11q23 were used as the reference group (HR = 1.10;  $P = 0.53$ ), further confirming that t(9;11) was an intermediate cytogenetic risk factor. Similar results were observed for EFS when patients with unfavorable or intermediate risk non-11q23 AML were used as the reference group (HR = .52;  $P < 0.001$  and HR = 1.04;  $P = 0.80$ , respectively).

In multivariate analysis, there was no significantly different in OS in group t(6;11), t(11;19), unbalanced 11q23, ort(11;v)(q23;v) group (HR = 1.17, 0.72, 0.97 and 0.84, respectively;  $P = 0.62, 0.20, 0.85$  and  $0.59$ , respectively; Table 2) when compared to patients with unfavorable non-11q23 AML, indicating they were independent poor prognostic factors for OS. These were further confirmed by comparing to patients with intermediate non-11q23 AML. Of note, the presence of t(11;19) and t(11;v)(q23;v) was a marginally significant factor for poor OS ( $P = 0.07$ ; Table 2) when patients with intermediate non-11q23 AML were used as reference group. Similar results were observed for EFS when patients with unfavorable non-11q23 AML were used as the reference group (Table 2). Of note, when

compared to patients with intermediate non-11q23 AML, only t(6;11) and unbalanced 11q23 aberrations were independent poor prognostic features for EFS (HR=2.00,  $P=0.02$  and HR=1.58,  $P=0.005$ , respectively).

### Molecular abnormalities in cases of 11q23 AML

The incidence of *RAS* mutations was slightly higher in the 11q23 AML group than in the non-11q23 AML reference group [21.8% (12/55) and 18.3% (203/1112), respectively ( $P=0.48$ )]. However, *FLT3*-ITD mutations were detected in 4.8% (3/63) and 16.1% (226/1406;  $P=0.01$ ) of the 11q23 and non-11q23 groups, respectively; *FLT3*-D835 mutations were detected in 6.4% (4/63) and 5.0% (70/1405;  $P=.55$ ), respectively; and *NPM1* mutations were detected in 2.9% (1/35) and 20.7% (114/552;  $P<0.001$ ), respectively. These results are consistent with other reports, thereby indicating that 11q23 AML often harbors gene mutations involved in the *RAS* pathway,<sup>21</sup> whereas mutations in *FLT3* and *NPM1* are uncommon.<sup>21–23</sup>

### Role of allogeneic SCT in post remission consolidation at CR1

Of the 98 AML patients with 11q23 abnormalities who achieved CR after induction chemotherapy. Donor availability for four patients is unknown. Among remaining 94 patients, 55 patients had no donor or were not screened for donor, 39 patients (41%) had donor available. Patient characteristics by donor vs. non-donor were shown in Table 3. The clinical characteristics of the patients with donor vs. non-donor were well balanced except patient age, bone marrow blast and 11q23 aberrations. Of 39 patients, 24 underwent allogeneic SCT (16 from related donors, 4 from unrelated donors, 3 cord blood, and 1 from a haploidentical donor) in CR1. The conditioning regimens consisted of fludarabine plus busulfan ( $n=14$ ), fludarabine plus melphalan ( $n=8$ ), Total body irradiation plus etoposide and cyclophosphamide ( $n=1$ ), or unknown regimen ( $n=1$ ). The median time from CR1 to SCT was 3 months (range, 1 to 27 months). Patients who underwent allo-SCT at CR1 ( $n=39$ ) had a significantly longer OS ( $P<0.001$ ) and RFS ( $P<0.001$ ) than those who did not undergo allo-SCT at CR1 ( $n=55$ ; Figure 3A and 3B). This superior outcome was also evident when considering only patients with t(9;11) (Figure 3C and 3D). Multivariate analysis using allo-SCT as a time-dependent covariable after controlling for other risk factors as described above revealed a significant positive impact of allo-SCT at CR1 on OS (HR=0.56;  $P=0.02$ ) and RFS (HR=0.51;  $P=0.01$ ; data not shown).

## DISCUSSION

The results of the current study of a large cohort of patients confirm that AML with t(9;11) is indeed a distinct entity with a better clinical outcome than AML with other 11q23 abnormalities. In multivariate analysis, t(9;11) was the only independent predictor of survival with the OS and EFS of these patients being comparable to those of patients with intermediate cytogenetic risk (HR 1.10 and 1.04, respectively; Table 2). These results are in agreement with those reported in previous studies of 47 adult patients with de novo AML by the Cancer and Leukemia Group B<sup>18</sup> and of 180 adult patients with AML by the German AML Intergroup<sup>16</sup> and in a more recent study by the Medical Research Council, which showed that the prognosis of these patients was better than that of patients with other

balanced t(11q23).<sup>4</sup> Our data conflict with another study of 54 adult patients with AML that demonstrated no significant difference in prognosis between cases with t(9;11) (n=19) and cases with other balanced t(11q23) (unfavorable prognosis).<sup>17</sup> The reasons for the potential superior outcome of patients with t(9;11) compared to those with other MLL translocations are unknown and may be related to the differences of proteins encoded by MLL fusion genes derived from various translocations. Of note, t(9;11) is more commonly associated with t-AML/s-AML, but has the highest OS rate among 11q23 AML subgroups and non-11q23 AML reference group, this could be due to t(9;11) is less associated with del(5q)-5, del(7q)-7 and/or complex karyotype and also suggests that, at least in this population, t-AML/s-AML is a weak prognostic factor.<sup>24</sup>

In our study, patients with t(6;11), like those with t(9;11), presented at a younger age and with a higher percentage of bone marrow blasts than patients with non-11q23. However, t(6;11) was shown to be an independent poor prognostic feature in adult AML (Tables 2). Adverse outcomes of patients with t(6;11) have been reported in pediatric AML<sup>12</sup> and adult AML by Cancer and Leukemia Group B<sup>15</sup> and the German AML Intergroup.<sup>16</sup> Given the dismal outcomes of these patients, clinical trials using novel strategies should be encouraged for this group.

Group t(11;19) had the lowest incidence of del5/5q-, del7/7q- and/or complex karyotypes (6%) among 11q23 subgroups and the non-11q23 reference group, and is not commonly associated with t-AML/s-AML. However, t(11;19) was also identified as an independent adverse prognostic feature in adult AML, a finding that is consistent with the results reported in the majority of other such studies<sup>16, 17, 25</sup> but that conflicts with the findings of a recent study by the Medical Research Council.<sup>4</sup>

The various other unbalanced 11q23 aberrations were the second most common 11q23 abnormalities, and the majority of the cases in this group had del(11)(q23). This group was commonly associated with del5/5q-, del7/7q-, and/or complex karyotypes and a poor prognosis. Del(11)(q23) and inv 11q23 aberrations have been described involving the human MLL gene and several translocation partner genes have been identified for each of them.<sup>26-30</sup> The prognostic significance of unbalanced 11q23 aberrations was first reported in a smaller study.<sup>31</sup> In present study, we confirmed that the presence of unbalanced 11q23 aberrations is an independent poor prognostic factor. The subset of cases with other balanced translocations involving 11q23 was small, and the prognosis of this group was similar to that of the patients with unfavorable risk in the non-11q23 reference group.

In this study of allo-SCT for AML patients with 11q23 abnormalities, we demonstrated that all-SCT in CR1 results in sustained remission and long-term survival for approximately 40% of patients. Allo-SCT significantly improved OS and RFS compared with no allo-SCT. A majority of AML patients with 11q23 abnormalities who received consolidation with chemotherapy relapsed and died within a year and 5-year OS and RFS is 13% and 10% respectively. We also observe that there is a plateau in the OS and RFS curves, suggesting the allo-SCT could be a curative for these rare diseases. In multivariate analysis, we revealed a significant impact of allogeneic SCT in CR1 on OS ( $P=0.02$ ) and RFS ( $P=0.01$ ) in patients with 11q23 aberrations. In the last decade, the number of allo-SCT has increased

significantly.<sup>32</sup> In a recent study of 3638 patients with AML using meta-analysis, investigators revealed a significant survival benefit of allo-SCT from matched sibling donor for AML patients with unfavorable and intermediate cytogenetic risk groups.<sup>33</sup> Two other studies showed that allo-SCT from HLA-matched unrelated donor and matched sibling donor yield similar clinical outcomes in patients with high risk AML.<sup>34, 35</sup> Our results are in line with these studies, but contradict a recent report of 49 patients with AML and 11q23 abnormalities who received allo-SCT at CR1, in which allogeneic SCT had only borderline significant impact on OS.<sup>16</sup>

In summary, we found characteristic differences among patients with different 11q23 aberrations, which may suggest differences in etiology; we confirmed that in adult AML, t(9;11) is an intermediate risk factor, whereas, t(6;11), t(11;19), unbalanced 11q23 aberrations, and t(11;v)(q23;v) all had dismal outcomes; the presence of del5/5q-, del17/7q-, and/or complex karyotypes confers a poorer prognosis in patients with 11q23 AML. Most importantly, we revealed that allo-SCT provides significant OS and RFS benefits for patients with 11q23 AML in CR1. Innovative treatment strategies should be investigated in adults with these cytogenetic abnormalities.

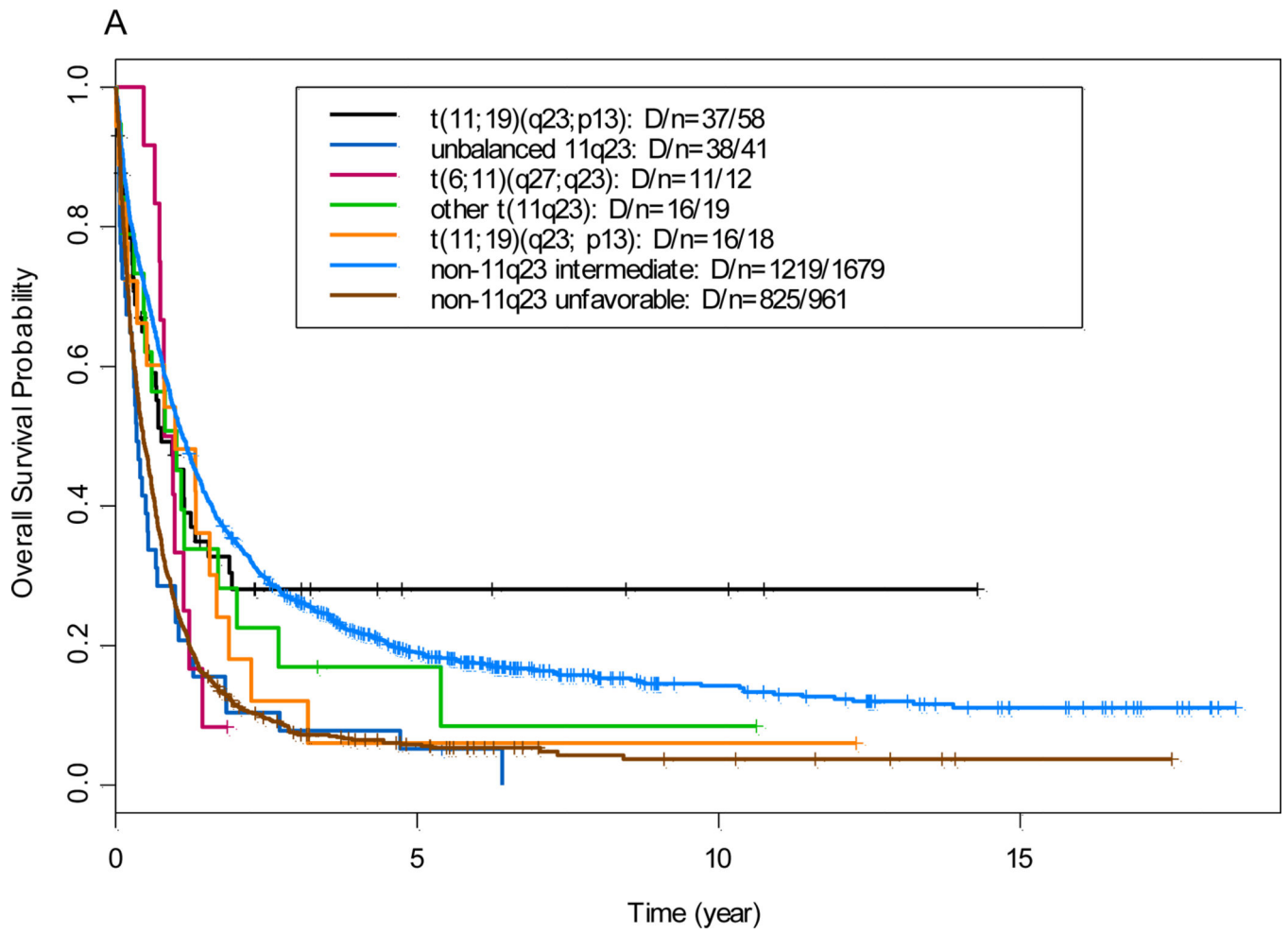
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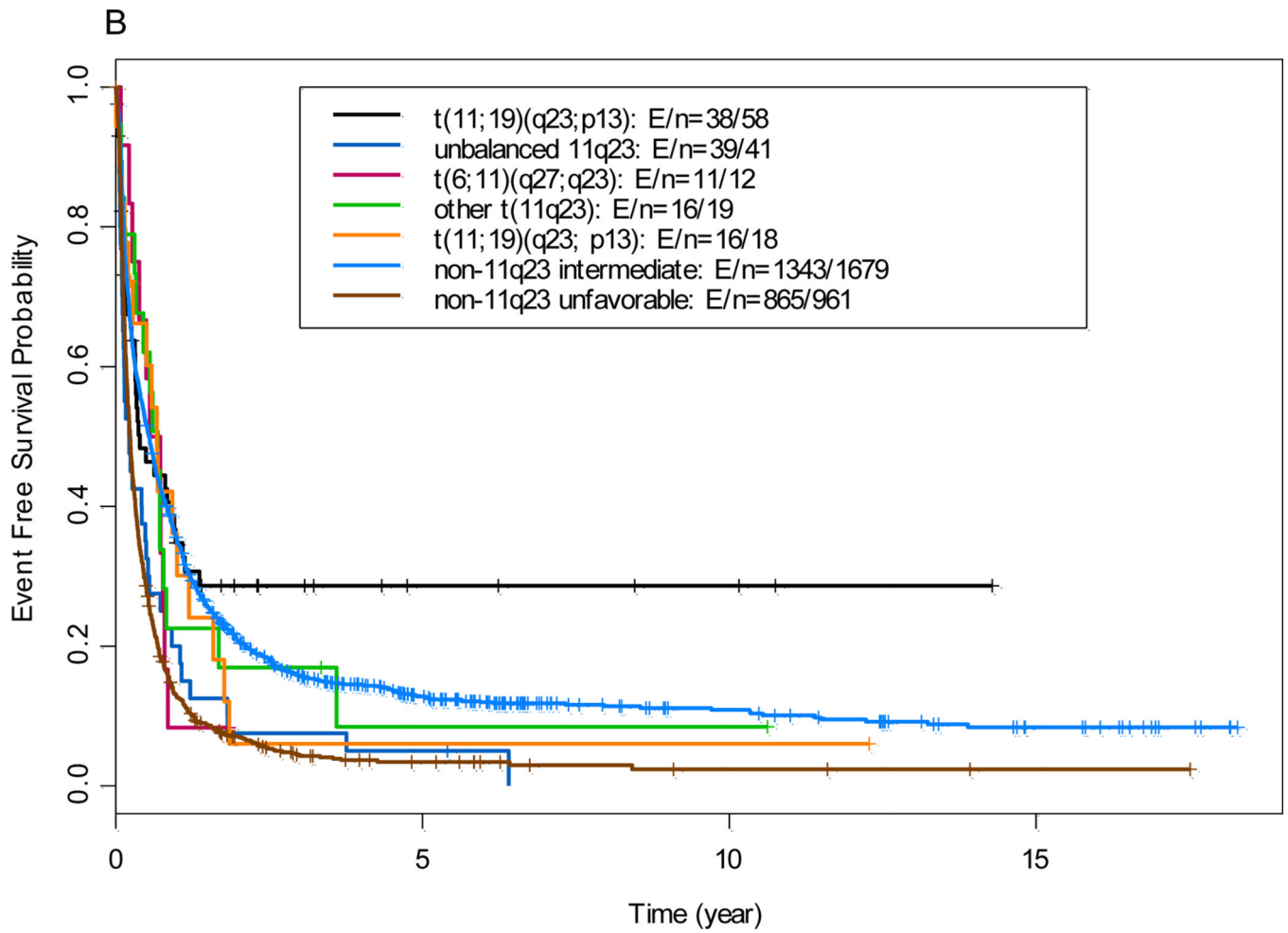
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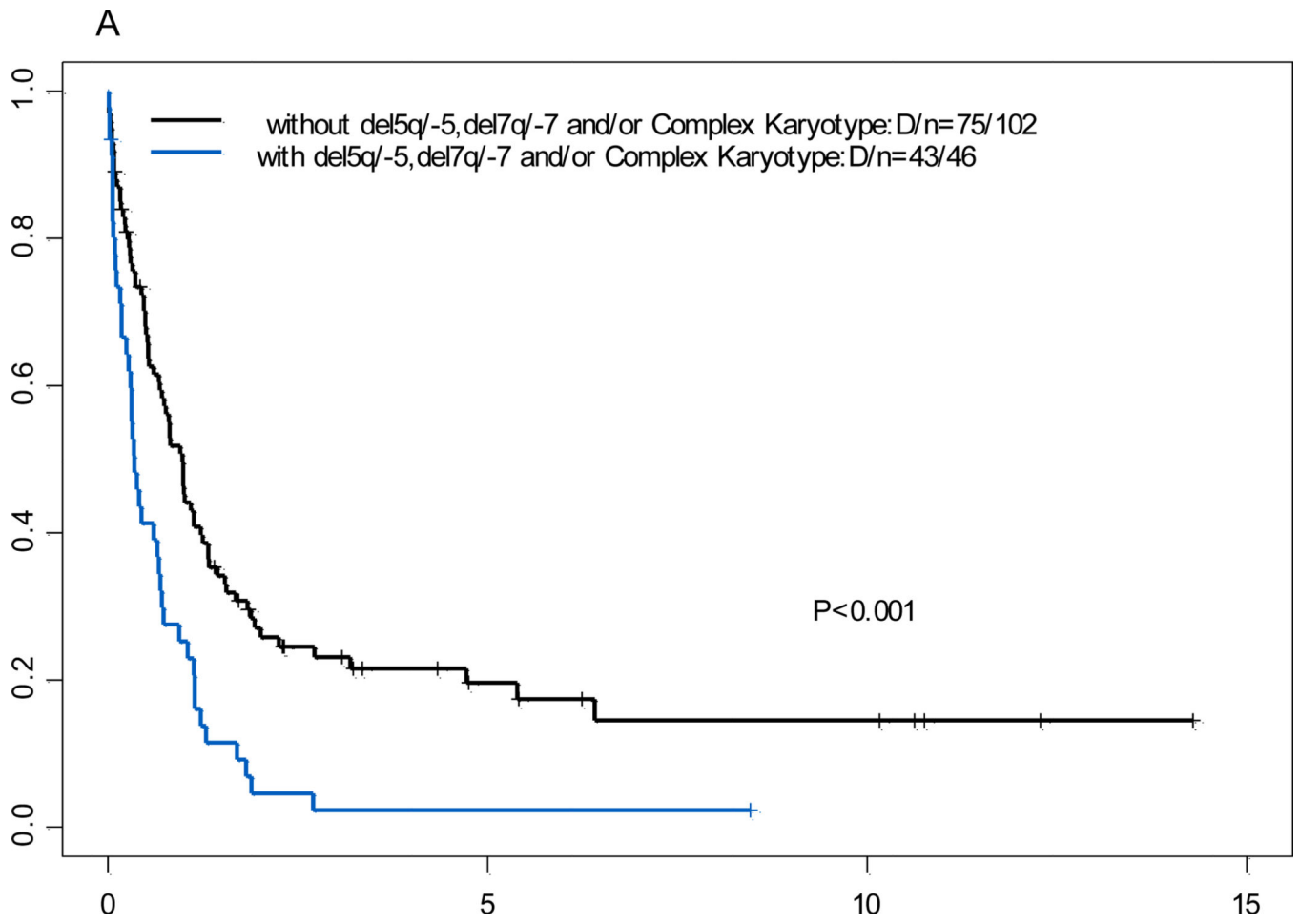


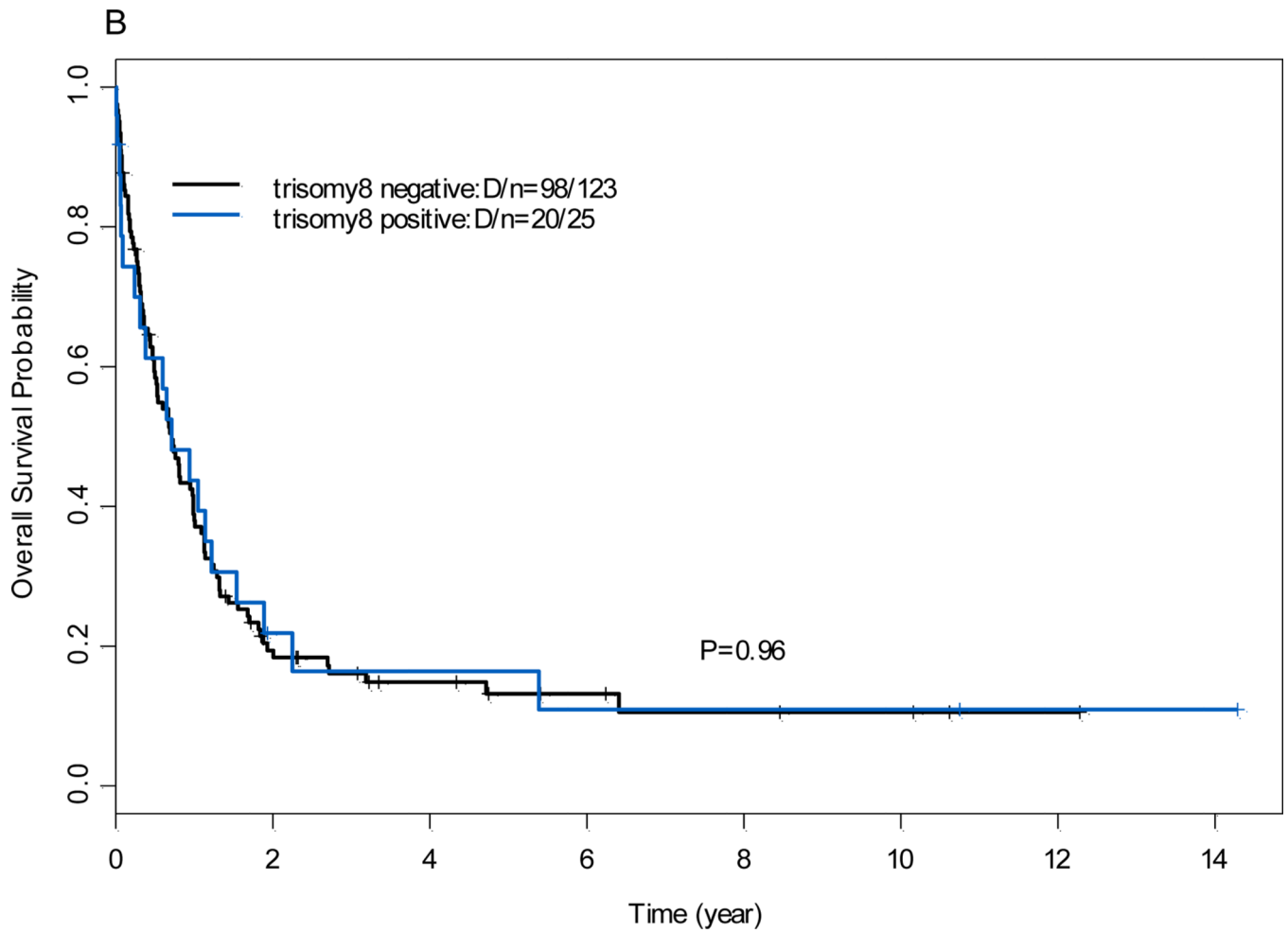


**Figure 1.**

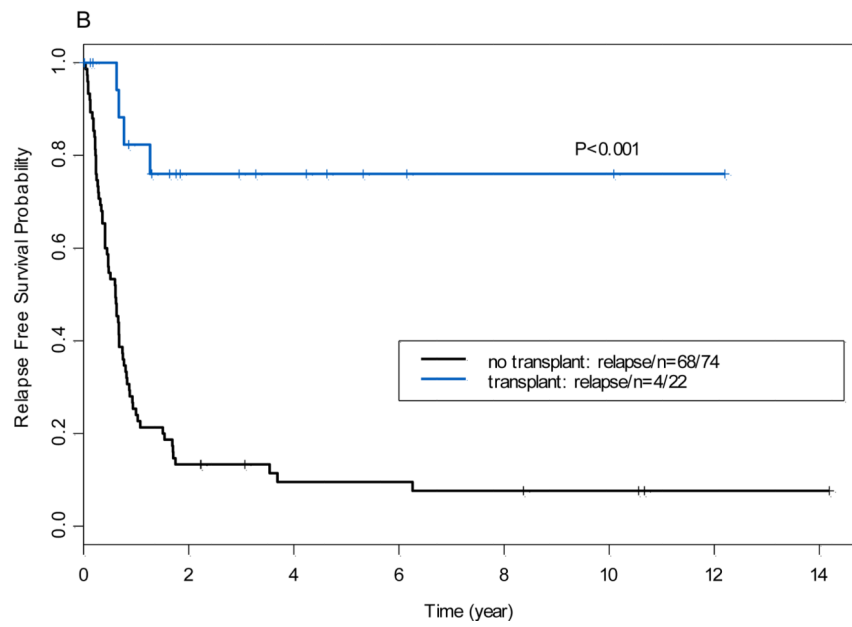
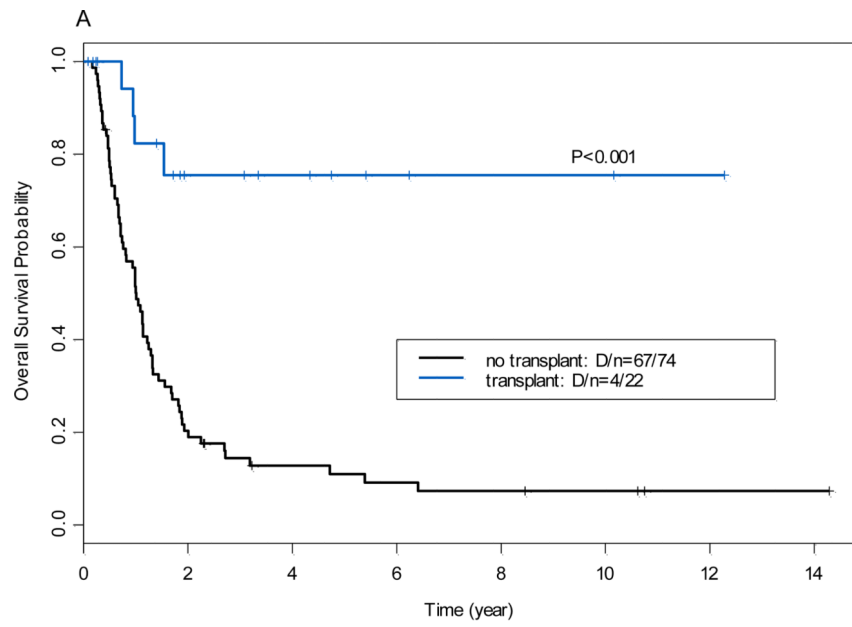
(A) Overall survival by comparison of 11q23 subgroups with non-11q23 reference groups.

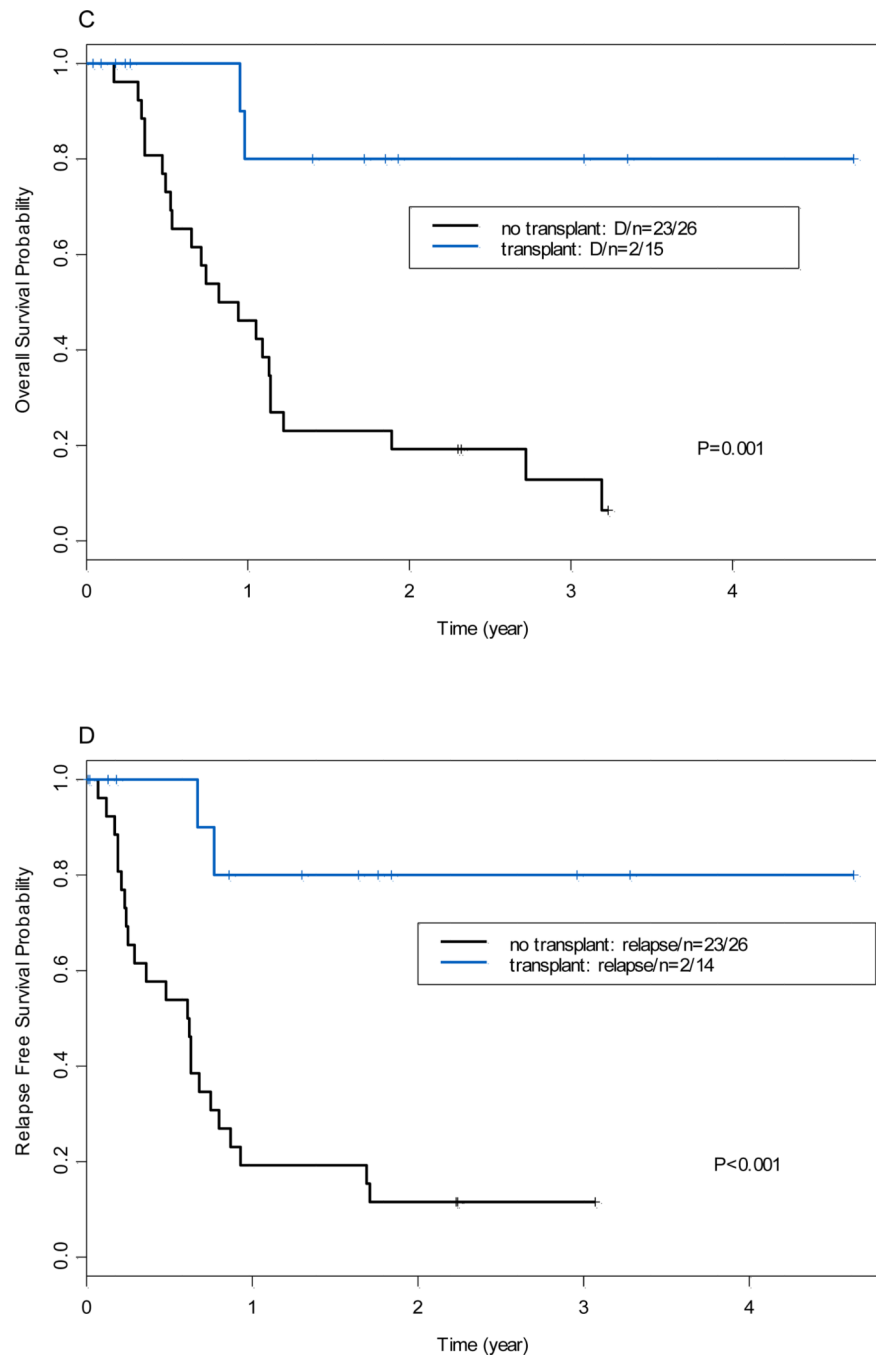
(B) Event-free survival by comparison of 11q23 subgroups with non-11q23 reference groups





**Figure 2.** Overall survival for 11q23 acute myeloid leukemia patients with or without del5/5q-, del7/7q- and/or complex karyotype



**Figure 3.**

(A) Overall survival by donor availability at first complete remission (all patients with 11q23). (B) Relapse-free survival by donor availability at first complete remission (all patients with 11q23). (C) Overall survival by donor availability [patients with t(9;11) only]. (D) Relapse-free survival by donor availability [patients with t(9;11) only]



**Table 1**  
Patient characteristics, response and outcomes by comparison of five 11q23 subgroups with non-11q23 reference group

Characteristic	Group t(9;11) (n=65)	Group t(6;11) (n=12)	Group t(11;19) (n=18)	Group unbalanced 11q23 (n=41)	Group t(11;v)(q23;v) (n=12)	Reference (unfavorable or intermediate, n=2640)	P*
Age, years	51 (17–77)	52 (31–62)	66 (31–81)	63 (22–84)	43 (21–65)	63 (14–93)	<0.001
P#	<0.001	0.002	1.0	0.5	<0.001		
WBC, × 10 <sup>9</sup> /L	10.3 (0.6–193.6)	9.3 (1.0–111.7)	6.4 (0.8–44.7)	4.3 (0.7–94.5)	10.1 (0.6–95.4)	6.1 (0.2–433)	0.64
Platelet, × 10 <sup>9</sup> /L	42 (7–194)	44 (20–155)	45 (10–112)	54 (7–199)	52 (25–192)	50 (1–2292)	0.98
HGB, g/dl	8.4 (4.6–14.4)	9.1 (6.6–10.5)	8.0 (4.3–11.2)	8.0 (5.1–14.1)	8.8 (4.7–11.8)	8.2 (2.0–15.1)	0.46
BM Blast (%)	81 (20, 98)	84 (42, 94)	53 (18, 92)	50 (17, 92)	75 (21, 94)	43 (0, 98)	<0.001
P#	<0.001	<0.001	0.64	0.62	0.04		
Race, white	51 (79)	5 (42)	13 (72)	33 (81)	11 (92)	2131 (81)	0.04
P#	0.4	0.003	0.37	1.0	0.15		
t-AML/s-AML	33 (51)	1 (8)	6 (33)	16 (39)	2 (17)	909 (34)	0.02
P#	0.008	0.007	1	0.62	0.24		
FAB							
M4	13 (21)	3 (25)	5 (28)	6 (17)	2 (18)	383 (18)	
M5	38 (60)	6 (50)	5 (28)	8 (23)	3 (27)	159 (8)	
others	12 (19)	3 (25)	8 (44)	21 (60)	6 (55)	1582 (75)	<0.001
P#	<0.001	<0.001	0.004	0.009	<0.001		
Del(5q)-5, del(7q)-7 and/or Complex Karyotype	13 (20)	2 (17)	1 (6)	27 (66)	5 (42)	939 (36)	<0.001
P#	0.008	0.23	0.006	<0.001	1.0		
Trisomy8	14 (22)	1 (8.3)	1 (6)	8 (20)	1 (8)	222 (8)	0.004
P#	0.003	1	1	0.02	0.21		
Gender, male	20 (31)	4 (33)	10 (56)	22 (54)	5 (42)	1562 (59)	
P#	<0.001	0.08	0.81	0.52	0.06		<0.001
CR rate	44 (68)	10 (83)	13 (72)	20 (49)	11 (92)	[370 (39) and 982 (60), respectively]	<0.001
5-year OS	27	0	6	5	18	(6 and 19, respectively)	<0.001

Characteristic	Group t(9;11) (n=65)	Group t(6;11) (n=12)	Group t(11;19) (n=18)	Group unbalanced 11q23 (n=41)	Group t(11;v)(q23;v) (n=12)	Reference (unfavorable or intermediate , n=2640)	<i>P</i> <sup>*</sup>
5-year EFS	27	0	6	5	0	(3 and 13, respectively)	<0.001

Note: AML with 11q23 abnormalities were defined as 5 groups: t(9;11), t(6;11), t(11;19), unbalanced 11q23 and t(11;v)(q23;v).

WBC indicates white blood cell; HGB, hemoglobin; BM, bone marrow; FAB, French-American-British Classification; CR, complete remission; OS, overall survival; EFS, event-free survival.

\* Kruskal-Wallis or Fisher exact test.

# Wilcoxon rank-sum test or Fisher's exact test. If the *P* values in right hand column were significant, we then compared the data from each 11q23 subgroup to the non-11q23 reference group and listed the *P* values below the row.

Table 2

Multivariate analysis of prognosis of five 11q23 subgroups

Variable	Overall Survival			Event-Free Survival		
	HR	95% CI	P	HR	95% CI	P
Using unfavorable as reference group						
AGE	1.03	1.02 to 1.03	<0.001	1.02	1.01 to 1.02	<0.001
HGB	0.95	0.92 to 0.99	0.02	0.94	0.90 to 0.97	0.001
Log WBC	1.09	1.03 to 1.15	0.004	1.14	1.08 to 1.20	<0.001
Log platelet	0.77	0.71 to 0.83	<0.001	0.81	0.76 to 0.88	<0.001
BM blast	1.00	0.99 to 1.00	0.007	1.00	1.00 to 1.00	0.11
De novo (yes vs. no)	0.79	0.69 to 0.91	0.001	0.85	0.75 to 0.98	0.02
PS (3,4 vs. 0,1,2)	2.44	1.93 to 3.08	<0.001	1.94	1.55 to 2.44	<0.001
Group t(9;11)	0.61	0.43 to 0.85	0.004	0.52	0.37 to 0.73	<0.001
Group t(6;11)	1.17	0.64 to 2.14	0.62	0.95	0.52 to 1.74	0.87
Group t(11;19)	0.72	0.44 to 1.19	0.20	0.61	0.37 to 1.00	0.05
Group unbalanced 11q23	0.97	0.70 to 1.35	0.85	0.86	0.62 to 1.19	0.36
Group t(11;v)(q23;v)	0.84	0.45 to 1.58	0.59	0.69	0.37 to 1.30	0.25
Treatment type 2 vs. 1	0.70	0.55 to 0.89	0.003			
Treatment type 3 vs. 1	0.84	0.69 to 1.03	0.09			
Using intermediate as reference group						
Age, per 10 years	1.03	1.02 to 1.03	<0.001	1.02	1.02 to 1.02	<0.001
Log WBC	1.08	1.03 to 1.13	0.001	1.11	1.06 to 1.16	<0.001
Log platelet	0.91	0.86 to 0.97	0.004	0.93	0.87 to 0.99	0.02
De novo (yes vs. no)	0.80	0.71 to 0.90	<0.001	0.80	0.71 to 0.90	<0.001
PS (3,4 vs. 0,1,2)	2.03	1.63 to 2.53	<0.001	1.82	1.46 to 2.26	<0.001
Group t(9;11)	1.10	0.80 to 1.53	0.53	1.04	0.75 to 1.44	0.8
Group t(6;11)	2.28	1.25 to 4.14	0.01	2.00	1.10 to 3.65	0.02
Group t(11;19)	1.59	0.97 to 2.61	0.07	1.19	0.73 to 1.96	0.49
Group unbalanced 11q23	2.01	1.45 to 2.79	<0.001	1.58	1.15 to 2.19	0.005
Group t(11;v)(q23;v)	1.77	0.95 to 3.31	0.07	1.45	0.77 to 2.71	0.25

Variable	Overall Survival			Event-Free Survival		
	HR	95% CI	P	HR	95% CI	P
Treatment type 2 vs. 1	0.83	0.68 to 1.00	0.05	0.93	0.77 to 1.11	0.42
Treatment type 3 vs. 1	1.29	1.09 to 1.52	0.003	1.55	1.32 to 1.82	<0.001
BM blast				1.00	1.00 to 1.00	0.01
HGB				0.93	0.91 to 0.96	<0.001

Note: AML with 11q23 abnormalities were defined as 5 groups: t(9;11), t(6;11), t(11;19), unbalanced 11q23 and t(11;v)(q23;v). Treatment type1, High-dose ara-C based regimens (HDAC); type2, non-HDAC based regimens; type 3, other non-ara-C based regimens.

WBC, white blood cell; HGB, hemoglobin; BM, bone marrow.

**Table 3**

Patient characteristics and outcomes by donor availability in first remission

Parameter		No donor available (n= 55)	Donor available (n=39)	P
Age, years	Median (range)	54 (20, 82)	49 (17, 67)	0.02
WBC, × 10 <sup>9</sup> /L	Median (range)	7.2 (0.6, 111.7)	3.8 (0.6, 73.7)	0.29
Platelet, × 10 <sup>9</sup> /L	Median (range)	39 (7, 199)	58 (8, 189)	0.17
HGB, g/dl	Median (range)	8.1 (4.3, 14.1)	8.5 (6, 14.4)	0.32
BM Blast (%)	Median (range)	64 (21, 96)	83 (20, 98)	0.03
t-AML/s-AML		24(43.6%)	15(38.5%)	0.67
Del(5q)/-5, del(7q)/-7 and/or Complex Karyotype		19(34.5%)	6(15.4%)	0.06
Gender, male		25(45.5%)	14(35.9%)	0.4
11q23 aberrations				0.03
t(9;11)		23(41.8%)	21(53.8%)	
t(6;11)		3(5.5%)	7(17.9%)	
All other 11q23 aberrations		29(52.7%)	11(28.2%)	
5-year overall survival	Median (range)	0.13 (0.06, 0.25)	0.39 (0.26, 0.58)	<0.001
5-year relapse-free survival	Median (range)	0.10 (0.05, 0.23)	0.40 (0.27, 0.59)	<0.001

Note: WBC, white blood cell; HGB, hemoglobin.