haematologica
Journal of the Ferrata Storti Foundation

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Received: August 28, 2025.
Accepted: June 17, 2026.

Citation: Iman Abou Dalle, Jacques-Emmanuel Galimard, Ali Bazarbachi, Regis Peffault de Latour, Patrice Chevallier, Peter Dreger, Gitte Olesen, Ibrahim Yakoub-Agha, Jurjen Versluis, Jürgen Kuball, Igor-Wolfgang Blau, Sandrine Loron, Thomas Heinicke, Dominik Schneidawind, Tobias A.W. Holderried, Keith Wilson, Thomas Schroeder, Frederic Baron, Eolia Brissot, Jordi Esteve, Arnon Nagler, Mohamad Mohty and Fabio Ciceri. Prognostic impact of t(9;11) and del(7q) as intermediate-risk abnormalities in acute myeloid leukemia following allo-transplant: an Acute Leukemia Working Party study from the European Society for Blood and Marrow Transplantation.
Haematologica. 2026 June 25. doi: 10.3324/haematol.2025.289080 [Epub ahead of print]

Prognostic impact of t(9;11) and del(7q) as intermediate-risk abnormalities in acute myeloid leukemia following allo-transplant: an Acute Leukemia Working Party study from the European Society for Blood and Marrow Transplantation

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Authors' Disclosures: The authors declare no conflicts of interest, and nothing to disclose.

Funding: This research had no funding

Authors Contributions: I.A wrote the manuscript with input from J-E G, MM, and AB. J-E G contributed to data collection and analysis. J-E G performed the statistical analysis of the data.

I.A., M.M, F.C and A.B., designed the study. All authors (R.PL, P.C, P.D, G.O, I. Y-A, J.V, J.K, I.W-B, S.L, T.H, D.S, T, H, K.W, T.S, F.B, E.B, J.E, A.N, F.C) participated in the discussion, intellectual content, and have reviewed and approved the final version of the manuscript.

Acknowledgments: We extend our sincere gratitude to the patients and their caregivers for their participation and trust. We also acknowledge the contribution of EBMT centers for providing data and continuous support in advancing transplant research. Special thanks to the EBMT statistical team and the support staff for their invaluable assistance in data collection, analysis, and interpretation.

Data Availability: The data analyzed in this study were provided and approved by the Acute Leukemia Working Party of the EBMT. All relevant data are provided within this manuscript. The relevant working party of the EBMT will review requests from qualified external researchers for data from the EBMT studies in a responsible manner that includes protecting patient privacy, assurance of data security and integrity, and furthering scientific and medical innovation. Additional details on the data sharing criteria and process for requesting access should be sent to ebmt.do-paris@ebmt.org. Individual patient data will not be shared.

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Abstract

The European LeukemiaNet (ELN) 2022 classification categorized both t(9;11)(p21.3;q23.3) and isolated del(7q) in acute myeloid leukemia (AML) as intermediate-risk when treated with intensive chemotherapy. However, their prognostic relevance in the context of allogeneic hematopoietic cell transplantation (allo-HCT) needs further validation. This retrospective, registry-based analysis from the EBMT assessed outcomes in adults with AML who underwent allo-HCT in first complete remission between 2010 and 2022.

In the first cohort, data from 141 patients with t(9;11) were analyzed, of whom 23% had additional adverse cytogenetic abnormalities (ACA), primarily complex karyotype. Most had *de novo* AML (72%), had received myeloablative conditioning (57%), and peripheral blood stem cells (88%). After a median follow-up of 3 years, there were no significant differences in 2-year relapse incidence (22% vs. 18.2%, p=0.85), leukemia-free survival (66% vs. 76%, p=0.42), or overall survival (72% vs. 75%, p=0.68) between patients with non-adverse t(9;11) and those with additional ACA.

The second cohort included 250 patients: 84 with del(7q), 95 with monosomy 7, and 71 with del(5q), and all without additional ACA. Most had *de novo* AML (59%) and had received reduced-intensity conditioning (65%). After similar follow-up, survival outcomes did not differ significantly across the groups (2-year leukemia-free survival: 61% vs. 59% vs. 52% for del(7q), monosomy 7 and del(5q), respectively).

In conclusion, these findings suggest that the prognostic value of t(9;11) as intermediate-risk remains consistent in the setting of allo-HCT regardless of additional ACA, whereas del(7q), even without additional ACA, confers a risk comparable to monosomy 7 and del(5q).

Introduction

The recently updated European LeukemiaNet (ELN) 2022 risk classification has redefined several genetic abnormalities and their associated risk categories in acute myeloid leukemia (AML) treated with intensive chemotherapy. The presence of t(9;11)(p21.3;q23.3) defines an intermediate-risk group, regardless of the presence of other, less common adverse cytogenetic abnormalities (ACA).[1] This classification reflects evidence that patients with t(9;11) often have clinical outcomes more favorable than those typically seen with translocations involving 11q23.[2] As such, the presence of t(9;11) takes precedence in risk assignment. Among the diverse group of *KMT2A* (originally *MLL*) rearrangements, t(9;11) is associated with a more favorable prognosis. This contrasts with other *KMT2A* translocations (e.g., t(6;11), t(10;11)), which are typically associated with poor outcomes. Clinical data from multiple studies, including those involving patients treated with intensive chemotherapy and allogeneic hematopoietic cell transplantation (allo-HCT), have shown that patients with t(9;11) have better complete remission rates, lower relapse risk, and improved survival compared to those with other adverse-risk features.[3, 4]

In addition, deletion of 7q (del(7q)) in the absence of additional ACA is classified as an intermediate-risk abnormality, whereas monosomy 7 (-7), the most frequent autosomal monosomy in AML, and del(5q) remain in the adverse-risk category.[1, 5, 6]

At the molecular level, haploinsufficiency of tumor suppressor genes located in the common deleted regions of chromosomes 5 and 7 has been implicated in the pathogenesis of myelodysplastic syndromes and AML.[7, 8] The genetic landscape of (-7) and del(7q) varies significantly depending on whether they occur as isolated lesions or within a complex karyotype (CK). Despite the well-recognized role of abnormalities of chromosome 5 and 7 in myeloid malignancies, studies investigating the impact of del(7q), (-7) and del(5q) in AML in the context of allo-HCT have been limited by heterogeneous study populations, often including additional ACA such as CK, which can interfere with clinical outcomes.

Therefore, it is imperative to further validate the prognostic implications of AML subgroups with t(9;11) and ACA, as well as del(7q) in comparison to (-7) and del(5q) without additional ACA in the setting of allo-HCT.

Methods

Study Design and Inclusion Criteria

This is a retrospective, registry-based analysis from the European Society for Blood and Marrow Transplantation (EBMT) with the approval of the Acute Leukemia Working Party (ALWP). The EBMT is a voluntary working group of more than 600 transplant centers that are required to report all consecutive HCTs and follow-ups once a year. Audits are routinely performed to

determine the accuracy of the data. Since January 2003, all transplant centers have been required to obtain written informed consent before data registration with the EBMT, following institutional review board committee approval abiding by the guidelines of the Declaration of Helsinki, 1975.

Adult patients aged more than 18 years with a diagnosis of AML who received an allo-HCT in first complete remission (CR1) between 2010 and 2022, with an available full karyotype at diagnosis, were included. We selected those with t(9;11) and any other associated abnormality for the first analysis, and del(7q), not classified as CK, or monosomal karyotype and without other ACA for the second analysis. These could be isolated or accompanied by an additional non-adverse cytogenetic abnormality. Patients with (-7) or del(5q) without other ACA were chosen as a comparative group for the second analysis. Cytogenetics was reported by full karyotype by the participating center, most often using the International System for Human Cytogenomic Nomenclature (ISCN) guidelines. The (-7), del(7q) and del(5q), were defined as the entire loss of chromosome 7, partial deletion of the long arm of either chromosome 7, or of chromosome 5. Cytogenetic abnormalities were categorized according to the ELN 2022 risk classification. ACA were defined as all chromosomal abnormalities classified as adverse risk by ELN 2022, including complex karyotype, monosomal karyotype, −5/del(5q), −7, abnormalities of 3q26.2 (e.g., inv(3)/t(3;3)), t(6;9)(p23;q34.1), t(v;11q23.3)/KMT2A rearranged (except t(9;11)), t(9;22), and other cytogenetic lesions designated as adverse in the ELN 2022 recommendations.

Variables collected included recipient age at transplant, recipient and donor gender, karyotype at diagnosis, *NPM1, FLT3*-ITD, and *CEBPA* mutation status at diagnosis, time from diagnosis to transplant, year of transplant, measurable residual disease (MRD) status at transplant, Karnofsky performance status score at transplant, HCT-specific comorbidity index, in addition to transplant-related factors including conditioning regimen, graft-versus-host disease (GVHD) prophylaxis, the use of post-transplant cyclophosphamide, *in-vivo* T cell depletion, donor type, recipient and donor cytomegalovirus status, and stem cell source (peripheral blood or bone marrow).

Endpoints and Statistical Analysis

Quantitative variables are described as median with a range of minimum and maximum. Qualitative variables are described as frequencies and percentages. Comparisons between groups were done using Wilcoxon Chi-square tests for quantitative and qualitative variables respectively.

Clinical endpoints included leukemia-free survival (LFS), overall survival (OS), non-relapse mortality (NRM), relapse incidence (RI), and GVHD outcomes. All outcomes were measured from the time of allo-HCT. LFS was defined as survival without leukemia relapse or progression; patients alive without leukemia relapse or progression were censored at the time of last contact. OS was defined as death from any cause. NRM was defined as death without previous

leukemia relapse. Death and relapse were competing events for GVHD outcomes. All events were censored at 2 years post allo-HCT due to different follow-up periods between groups.

The probabilities of LFS and OS were calculated using the Kaplan-Meier method and compared by Log-rank tests. Cumulative incidence functions were used to estimate RI, NRM and GVHD outcomes in a competing risk setting and compared with Gray test.

The impact of adverse cytogenetics on patients with t(9;11) cytogenetics was only compared with univariate tests due to low number of patients. For the comparison of del(5q), (-7) and del(7q), multivariable analyses was carried out using a Cox model to obtain the hazard ratio (HR) and 95% confidence interval (95% CI) and adjusted on type of AML (de novo/secondary), donor type, conditioning regimen used, age and year at transplant. All analyses were performed using R 4.1.1 (R Development Core Team, Vienna, Austria, URL:https://www.R-project.org/).

Results:

Analysis 1: t(9;11) +/- ACA

We identified 141 patients with t(9;11). Most of these patients had clinically defined *de novo* AML (72%), with a median age of 46 years (range: 19-71), and 60% were female. Patients received primarily myeloablative conditioning (57%) and peripheral blood stem cells (88%) from a matched sibling (25%), unrelated (38%), or haploidentical donor (14%). **(Table 1)**

Of these, 32 (23%) had ACA, mostly (75%) CK, followed by monosomy 7 (10%). There were no significant differences in baseline characteristics between those with or without additional ACA **(Table 1)**. The majority of patients in the intermediate and ACA categories had undetectable MRD (85% versus [vs.] 92%, respectively).

After a median follow-up of 3 years (95% CI: 2.1–3.2 years), there were no statistically significant differences observed in key post-transplant outcomes between patients with non-adverse t(9;11) and those with t(9;11) plus ACA **(Figure 1)**. Specifically, the 2-year RI was 22% (95% CI: 14–31%) in the t(9;11)-only group compared to 18.2% (95% CI: 6.4–35%) in the t(9;11)+ACA group (p = 0.85). The 2-year LFS rates were 66% (95% CI: 56–75%) vs. 76% (95% CI: 55–88%) for the two groups, respectively (p = 0.42). The 2-year OS was also not different, at 72% (95% CI: 62–80%) for patients with non-adverse t(9;11) and 75% (95% CI: 54–87%) for those with t(9;11)+ACA (p = 0.68). The survival outcomes remained comparable between patients with *de novo* AML and those with secondary AML, with no statistically significant differences observed between the two groups. **(Supplementary Figure 1)**

Analysis 2: del(7q) vs. (-7) vs. del(5q)

For the second analysis, we identified 250 patients, including 84 (34%) with del(7q), 95 (38%) with (-7) and 71 (28%) with del(5q), all without additional ACA **(Table 2)**. Most of these patients had clinically defined *de novo* AML (59%), with a median age of 59 years (range: 19-78), and 53% were female. Most patients received reduced-intensity conditioning (65%) and peripheral blood stem cells (90%) from a matched sibling (21%), unrelated (46%), or haploidentical donor (14%).

In general, there were no significant differences in baseline characteristics among the three subgroups apart from significantly more female patients in the del(5q) group (p=0.002). Among patients with del(7q), (-7), or del(5q), isolated abnormalities were observed in 58 (69%), 53 (56%) and 42 (59%) cases, respectively. Among patients with available mutation data, the majority were *NPM1*-negative (94%) and *FLT3*-ITD-negative (86%). Patients with del(7q) had a higher frequency of *FLT3*-ITD positivity (24%) compared to those with (-7) (8%) and del(5q) (9%). **(Table 2)**

After a median follow-up of 3 years, no significant differences were observed in the 2-year RI, LFS, OS, or NRM among patients with del(7q), (-7), or del(5q), without other ACA **(Figure 2)**. The 2-year RI was not different across the three subgroups: 24% for del(7q), 25% for (-7), and 29% for del(5q). When compared to del(7q), the HR for risk of relapse was 1.07 (95% CI: 0.54-2.13; p=0.85) for (-7) and 1.26 (95%CI: 0.63-2.55; p=0.51) for del(5q). Similarly, the 2-year LFS was 61% in patients with del(7q), 59% in those with (-7), and 52% with del(5q). The HR for LFS was 1.05 (95%CI: 0.62-1.78; p=0.86) for (-7) and 1.26 (95%CI: 0.74-2.16; p=0.40) for del(5q), indicating no statistically significant differences. The 2-year OS rates were also not different, with 69% for del(7q), 62% for (-7), and 65% for del(5q). The HR for OS was 1.13 (95% CI: 0.62-2.07; p=0.68) for (-7) and 1.02 (95% CI: 0.54-1.93; p=0.95) for del(5q) when compared to del(7q). Finally, the 2-year NRM was 14% in patients with del(7q), 16% in (-7) cases, and 19% in those with del(5q). The HR for NRM was 1.05 (95% CI: 0.45-2.45; p=0.91) for (-7), and 1.26 (95% CI: 0.53-2.99; p=0.60) for del(5q), further supporting the lack of significant differences in post-transplant outcomes across these cytogenetic subgroups, regardless whether AML was *de novo* or secondary in nature. **(Supplementary Table S1 and S2, Figure S2).**

Among the adjusting variables including cytogenetic subgroup, AML type, donor type, conditioning regimen, age at transplant (per 10-year increment), and year of transplant; the only factor significantly associated with a risk of worse OS was age at transplant. Each 10-year increase in age was associated with a 38% worse OS (HR: 1.38, 95% CI: 1.09–1.75; p=0.007). **(Supplementary Table S2).**

Discussion

In this multicenter study, we evaluated first the prognostic impact of additional ACA in patients with t(9;11) undergoing allo-HCT in CR1, mostly *de novo* AML. Our analysis shows that the

presence of additional ACA (predominately CK) does not significantly impact post-transplant outcomes. Among the 141 patients identified, nearly one-quarter harbored ACA, in line with prior studies reporting ACA in up to 40% of adult AML patients with KMT2A rearrangements. [9-11]

However, the lack of significant outcome differences between patients with non-adverse t(9;11) and those with t(9;11) + ACA in our analysis mirrors earlier findings, where survival outcomes did not appear to differ significantly based on ACA.[12, 13] Notably, Stölzel et al. reported that 8 of 10 patients with t(9;11) were categorized within the CK cohort with more than 4 abnormalities but still exhibited survival similar to those with normal karyotype, with a median OS of 23 months.[12]

An important consideration is the molecular landscape of KMT2A rearranged AML. While mutations in the RAS signaling pathway (*KRAS*, *NRAS*, *PTPN11*) are found in roughly 32% of KMT2Ar AML cases,[10] they appear to be far less frequent in t(9;11) patients, with some studies reporting rates as low as 3%.[14] Interestingly, in studies where *KRAS* mutations were more prevalent (up to 24%), patients with t(9;11) showed outcomes comparable to those with other fusion partners.[10, 11] These findings support the notion that molecular mutations, rather than ACA alone, may be more relevant to prognosis. In particular, *KRA*S mutations have been shown to confer an adverse prognostic impact in KMT2Ar AML.[13] Nevertheless, in the context of allo-HCT, such adverse features may be mitigated. Issa et al. reported that the negative prognostic impact of additional mutations was neutralized in multivariable models when allo-HCT was included, suggesting allo-HCT may override certain high-risk molecular characteristics.[3]

Our cohort was relatively young (median age 46 years), and the majority had *de novo* AML and achieved MRD-negative remission prior to transplant, features that likely contributed to the favorable outcomes observed. Prior studies have shown that younger adults (<60 years) with t(9;11) AML have superior outcomes compared to those with other KMT2A rearrangements.[14] However, the prognostic value of the fusion partner becomes less clear when older patients, therapy-related AML, or high-risk molecular features are included.[3] In such cases, the prognosis worsens, but our findings suggest that allo-HCT may help abrogate these adverse factors. Indeed, the 2-year OS in our cohort was 72% for all patients with t(9;11), regardless of age, AML type, and additional ACA.

In our second analysis, we demonstrated that AML patients with del(7q), mostly *de novo* AML, in the absence of additional ACA (classified as intermediate-risk in the ELN-2022) experience post-transplant outcomes comparable to those with (-7) or del(5q), in the absence of additional ACA (classified as adverse-risk in the ELN-2022). These three abnormalities could therefore be reclassified as one group, for which allo-HCT remains the most effective consolidation strategy, with approximately 50% of patients achieving prolonged disease-free survival.

The prognostic differences between (-7) and del(7q) remain a subject of debate. While some studies suggest that del(7q) confers a better prognosis than (-7), this finding has primarily been

observed in patients with myelodysplastic syndromes, some have reported worse outcomes with (-7), particularly due to a higher RI after allo-HCT. [15-17] In contrast, other studies have found no significant survival differences. [18, 19] In terms of clinical outcomes, relapse-free survival was significantly lower in patients with -7/non-CK compared to those with del(7q)/non-CK (p=0.048), with a suggestion of an inferior OS (P = 0.081). [20] However, when comparing AML patients with isolated (-7) vs. isolated del(7q), no significant differences in survival outcomes were observed.[20] Additionally, a study evaluating the impact of additional ACA on AML patients with -7/7q- after allo-HCT reported 2-year LFS rates of 48% for the "-7/7q- ± CK" group, compared to 36.4% for monosomal karyotype, 28.4% for del(5q), 19.1% for abnormalities involving 17p (abn(17p)), and 17.3% for inv(3) (p<0.001).[17] Within the "-7/7q- ± CK" cohort, (-7) was associated with a significantly higher RI compared to del(7q), leading to worse LFS, although OS was not significantly affected.[17] In this study, isolated abnormalities of -7 vs. del(7q) were not assessed. Despite these findings, clinical practice often consolidates (-7) and del(7q) into a single cytogenetic group, leading to a general recommendation for allo-HCT in CR1. However, direct comparisons between these subgroups remain limited, especially those with sole abnormalities of chromosomes 7 or 5, and the role of allo-HCT in these patients has not been systematically explored, thus the importance of our analysis.

Prior studies have highlighted significant genomic and prognostic differences between AML patients with (-7) and those with del(7q).[20-22] Among identified mutations, *KRAS* and *RUNX1* mutations were more frequently observed in -7/non-CK patients, while *FLT3* mutations were more common in del(7q)/non-CK cases, similar to our findings in the del(7q) subgroup.[20] A detailed mutational analysis revealed higher frequencies of *ASXL1*, *RUNX1*, *TET2* and *DNMT3A* mutations in AML patients with del(7q) compared to other AML subgroups, while *TP53* mutations were rare.[21, 23] Founder mutations affecting the *DNMT3A*, *ASXL1*, and *TET2* genes, were present in over 50% of cases with isolated (-7) or del(7q), with no significant differences in the overall somatic mutational landscape between these two subgroups. [19] These molecular findings further reinforce our results, supporting the conclusion that (-7) and del(7q) have similar clinical outcomes.

This study is strengthened by its real-world, multicenter nature and relatively large sample size for a rare cytogenetic entity. Nonetheless, it has limitations, including its retrospective design, lack of uniformity in MRD assessment methodologies, and absence of post-transplant maintenance therapy data, which could influence outcomes. The lack of data on whether patients received maintenance therapy, the type of agent used, duration of treatment, and adherence precludes adjustment for a potentially major modifier of post-transplant outcomes. This limitation is particularly relevant in the contemporary transplant era, where maintenance strategies are increasingly implemented in molecularly defined or high-risk subgroups and may substantially reduce relapse incidence. An additional key limitation of the present analysis is the absence of comprehensive molecular profiling, particularly for high-risk somatic mutations such as *TP53*, *ASXL1*, and *RUNX1*, which are known to exert a major influence on disease biology and post-transplant outcomes.

In conclusion, the presence of additional ACA in patients with t(9;11) does not appear to adversely impact risk of RI or survival outcomes following allo-HCT. This observation may require further confirmation in larger datasets with integrated molecular profiling. Additionally, del(7q), (-7), and del(5q), in the absence of other ACA such as CK or monosomal karyotype, confer similar clinical outcomes in the setting of allo-HCT. Interestingly, the observation that over 50% of these cases can be successfully salvaged with allo-HCT suggests that they may benefit from this approach in CR1. These findings suggest that the prognostic value of the t(9;11) as intermediate-risk remains consistent in the setting of allo-HCT, whereas del(7q) confers a comparable risk to monosomy 7 and del(5q).

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Table 1. Patient and transplant characteristics of the first analysis involving t(9;11) and t(9;11) with additional adverse cytogenetic abnormalities.

Variables	Modalities	N=141	Intermediate risk (n=109)	Adverse risk (n=32)	P-value
Age at HCT, y	median (range)	46 (19-71)	46 (19-71)	45 (19-67)	0.86
Patient sex	Female	84 (60)	62 (60)	22 (69)	0.23
Year of HCT	median (range)	2018 (2010-2022)	2018 (2010-2022)	2019 (2010-2022)	0.65
Months between diagnosis and HCT	median (range)	4.4 (2-19)	4.4 (2-15)	4.4 (2-19)	1
Cytogenetic abnormalities associated with t(9;11) 11q23, n (%)	Isolated With trisomy (8) With other abnormalities Complex_Monosomal Complex t(2;11) complex With abn(17p) mono(5) mono(7) With t(9;22)	63 (45) 30 (21) 16 (11) 1 (0.8) 24 (17) 1 (0.8) 1 (0.8) 1 (0.8) 3 (2) 1 (0.8)	63 (58) 30 (28) 16 (15) - - - - - - -	- - - 1 (3) 24 (75) 1 (3) 1 (3) 1 (3) 3 (10) 1 (3)	Not done
Type of AML, n (%)	de novo Secondary AML	102 (72) 39 (28)	79 (73) 30 (27)	23 (72) 9 (28)	0.95
MRD, n (%)	Positive Negative missing	7 (13) 45 (87) 89	6 (15) 34 (85) 69	1 (8) 11 (92) 20	1 f
NPM1, n (%)	Absent Present missing	50 (98) 1 (2) 90	36 (97) 1 (3) 72	14 (100) 0 (0) 18	1 f
FLT3ITD, n (%)	Absent Present missing	55 (92) 5 (8) 81	41 (93) 3 (7) 65	14 (88) 2 (12) 16	0.60 f
Female donor to male recipient, n (%)	Yes	18 (13)	16 (15)	2 (6)	
KPS, n (%)	< 90	41 (31)	35 (35)	6 (19)	0.11
Source of cells	PB BM Others	124 (88) 6 (4) 11 (8)	95 (87) 5 (5) 9 (8)	29 (91) 1 (3) 2 (6)	Not done
Donor type	Matched related Haploidentical Matched unrelated Other	35 (25) 19 (14) 53 (38) 34	28 (26) 14 (13) 42 (39) 25	7 (22) 5 (16) 11 (3) 9	Not done
Myeloablative regimen	Yes	80 (57)	60 (56)	20 (63)	0.49
PTCY, n (%)	Yes	20 (15)	16 (15)	4 (13)	1 f

Abbreviations: *HCT: hematopoietic cell transplantation; y: years; mono: monosomy; AML: acute myeloid leukemia; MRD: measurable residual disease; KPS: Karnofsky performance score; PB: peripheral blood; BM: bone marrow; PTCY: post-transplant cyclophosphamide*

Table 2. Patient and transplant characteristics of the second analysis involving del(7q), monosomy(7), and del(5q).

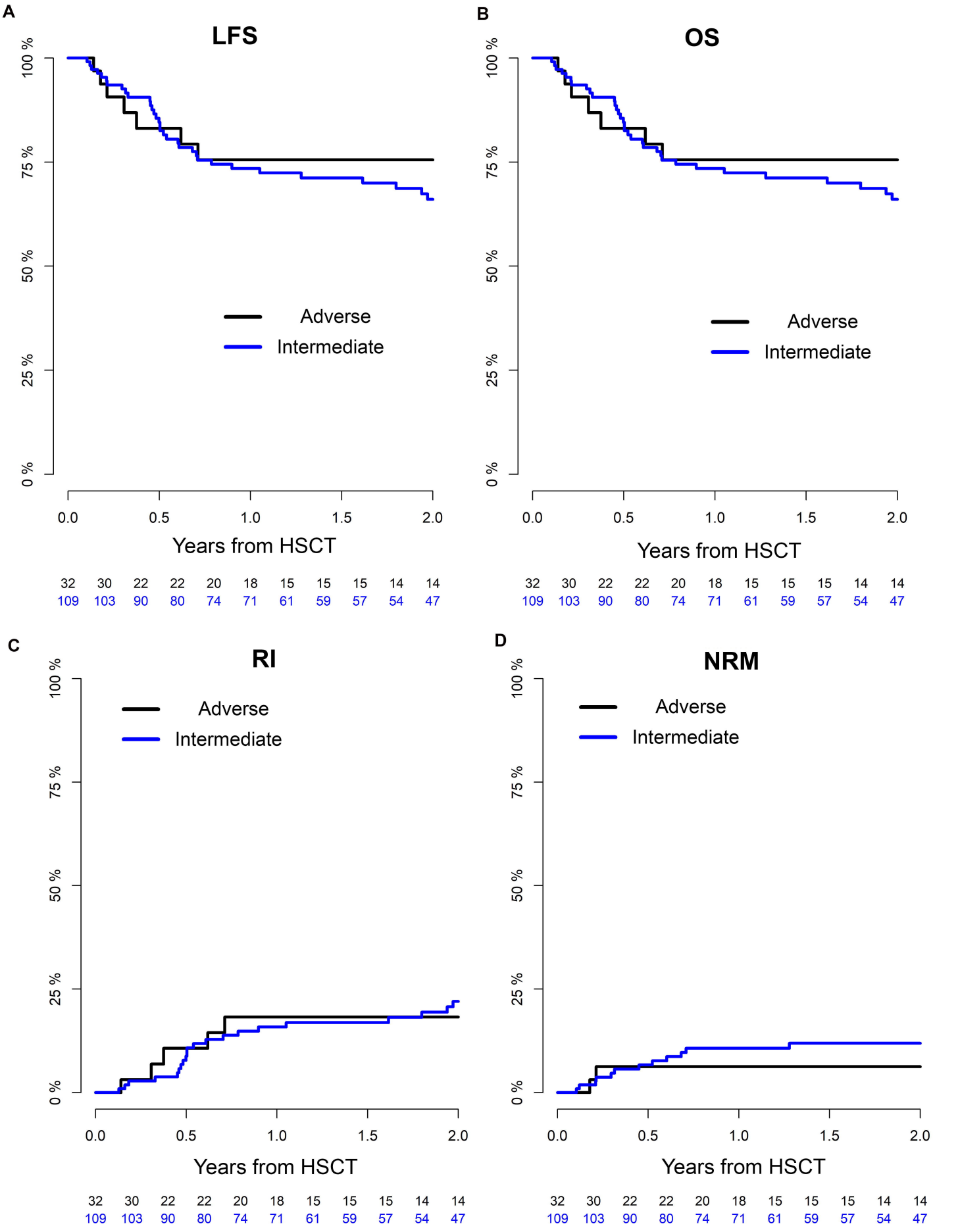
Variable	Modality	N=250	del(7q) (n=84)	(-7) (n=95)	del(5q) (n=71)	P-value
Age at HCT, y	Median (range)	59 (19-78)	59 (19-77)	58 (19-76)	63 (24-77)	0.11
Patient sex	Female	132 (53)	40 (48)	42 (44)	50 (70)	0.002
Year of HCT	Median (range)	2018 (2010-2022)	2019 (2010-2022)	2019 (2010-2022)	2018 (2010-2022)	0.12
Months between diagnosis and HCT	Median (range)	4.6 (1-57)	4.6 (2-57)	4.6 (1-18)	4.4 (2-19)	0.87
Cytogenetic abnormalities (not CK, not MK, without other adverse cytogenetic abnormalities, n (%)	del(7q) isolated del(7q) (-7) isolated (-7) del(5q) isolated del(5q)	58 (23) 26 (10) 53 (21) 42 (17) 42 (17) 29 (12)	58 (69) 26 (31) - - - -	- - 53 (56) 42 (44) - -	- - - - 42 (59) 29 (41)	Not done
Type of AML, n (%)	*de novo* Secondary AML	147 (59) 103 (41)	63 (75) 21 (25)	48 (51) 47 (49)	36 (51) 35 (49)	0.001
MRD, n (%)	Positive Negative missing	38 (40) 58 (60) 154	10 (26) 28 (74) 46	14 (47) 16 (53) 65	14 (50) 14 (50) 43	Not done
NPM1, n (%)	Absent Present missing	120 (94) 8 (6) 122	36 (90) 4 (11) 44	51 (96) 2 (4) 42	33 (94) 2 (6) 36	Not done
FLT3ITD, n (%)	Absent Present missing	121 (86) 19 (14) 110	35 (76) 11 (24) 38	48 (92) 4 (8) 43	38 (91) 4 (9) 29	Not done
Female donor to male recipient	Yes	29 (12)	11 (13)	12 (13)	6 (8)	
KPS, n (%)	< 90	70 (30)	22 (27.5)	28 (32)	20 (29)	0.79
Source of cells, n (%)	PB BM Other	224 (90) 20 (8) 6 (2)	78 (93) 4 (5) 2 (2)	81 (85) 12 (13) 2 (2)	65 (92) 4 (6) 2 (2)	Not done
Donor type, n (%)	Matched related Haploidentical Matched unrelated Other	52 (21) 36 (14) 114 (46) 48 (19)	24 (29) 10 (12) 36 (42) 14 (17)	15 (16) 15 (16) 47 (49) 18 (19)	13 (18) 11 (15) 31 (44) 16 (23)	Not done
Myeloablative regimen, n (%)	Yes	88 (35)	26 (31)	40 (43)	22 (31)	0.2
PTCY, n (%)	Yes	46 (18)	12 (14)	15 (16)	19 (27)	

Abbreviations: *HCT: hematopoietic cell transplantation; y: years; CK: complex karyotype; MK: monosomal karyotype; AML: acute myeloid leukemia; MRD: measurable residual disease; KPS: Karnofsky performance score; PB: peripheral blood; BM: bone marrow; PTCY: post-transplant cyclophosphamide.*

Figure Legends:

Figure 1: Survival Outcomes for First Analysis: (A) Leukemia-free survival (B) Overall survival (C) Relapse incidence (D) Non-relapse mortality by cytogenetic subgroup [t(9;11) vs. t(9;11)+additional adverse cytogenetic abnormalities]

Figure 2: Survival Outcomes for Second Analysis: (A) Leukemia-free survival (B) Overall survival (C) Relapse incidence (D) Non-relapse mortality by cytogenetic subgroup [del(7q), (-7), and del(5q)].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Years from HSCT
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109 103 90 80 74 71 61 59 57 54 47
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Years from HSCT
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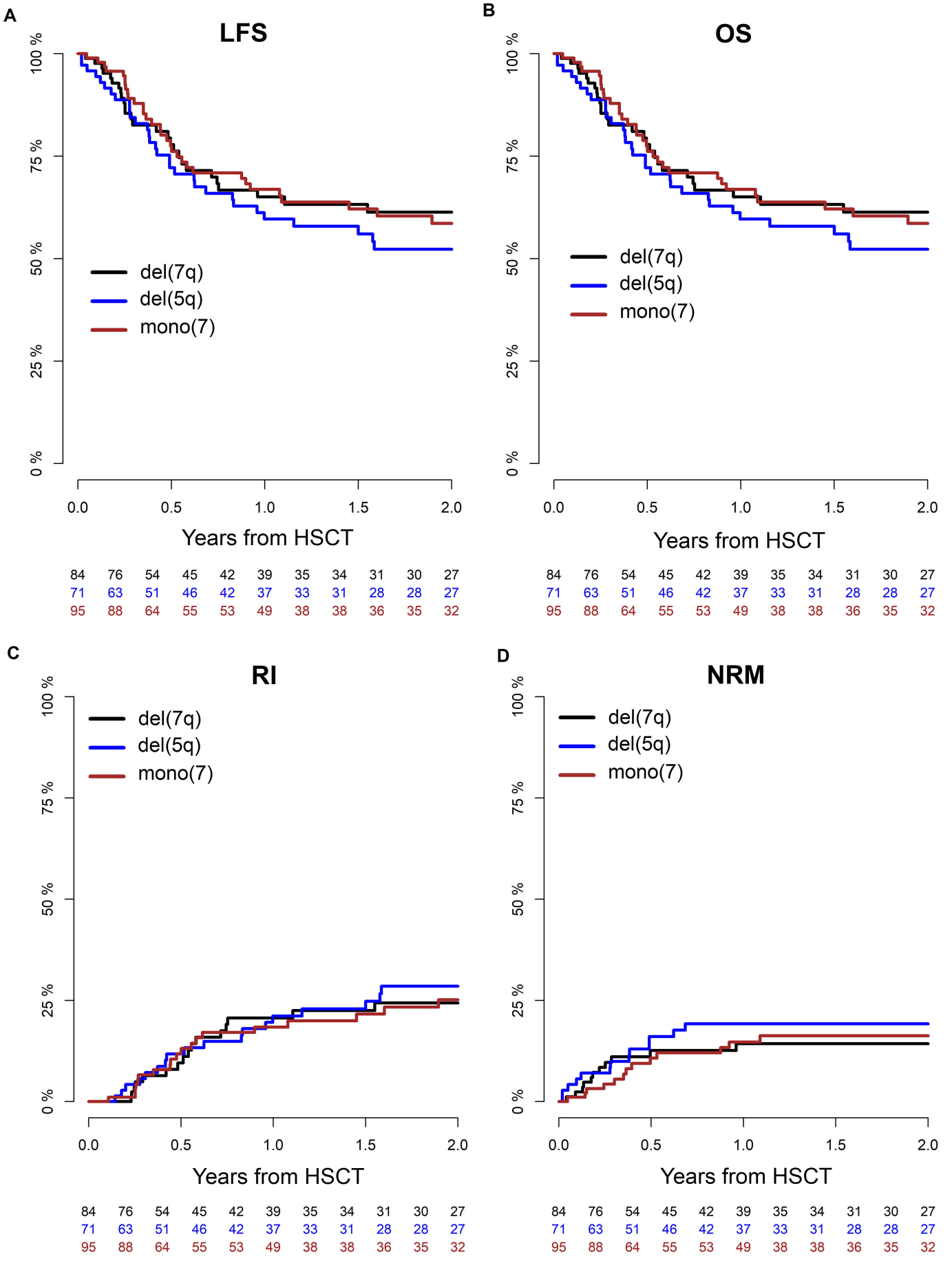
109 103 90 80 74 71 61 59 57 54 47


A
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del(7q)
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Years from HSCT
84 76 54 45 42 39 35 34 31 30 27
71 63 51 46 42 37 33 31 28 28 27
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Years from HSCT
84 76 54 45 42 39 35 34 31 30 27
71 63 51 46 42 37 33 31 28 28 27
95 88 64 55 53 49 38 38 36 35 32
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Years from HSCT
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71 63 51 46 42 37 33 31 28 28 27
95 88 64 55 53 49 38 38 36 35 32
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Years from HSCT
84 76 54 45 42 39 35 34 31 30 27
71 63 51 46 42 37 33 31 28 28 27
95 88 64 55 53 49 38 38 36 35 32

Prognostic impact of t(9;11) and del(7q) as intermediate-risk abnormalities in acute myeloid leukemia following allo-transplant: an Acute Leukemia Working Party study from the European Society for Blood and Marrow Transplantation

Supplementary Material

Figure S1. (1) Leukemia-free survival (2) Overall survival (3) Relapse Incidence (4) non-relapse mortality by cytogenetic abnormality [t(9;11) vs. t(9;11)+additional adverse cytogenetic abnormalities] and AML subtype (de novo versus secondary)

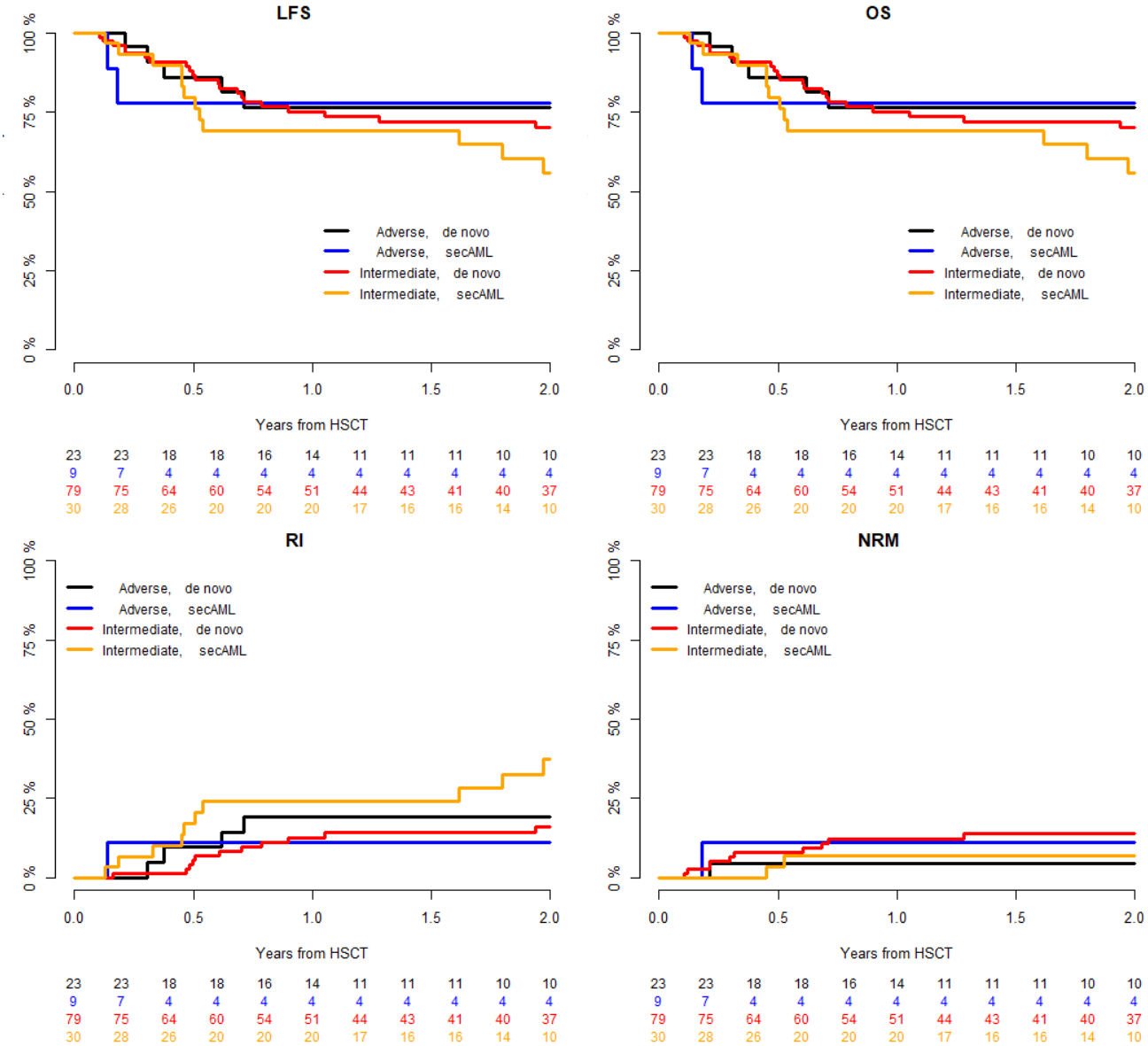

Figure S2. (1) Leukemia-free survival (2) Overall survival (3) Relapse Incidence (4) non-relapse mortality by cytogenetic abnormality [del(7q), (-7), and del(5q)] and AML subtype (de novo versus secondary)

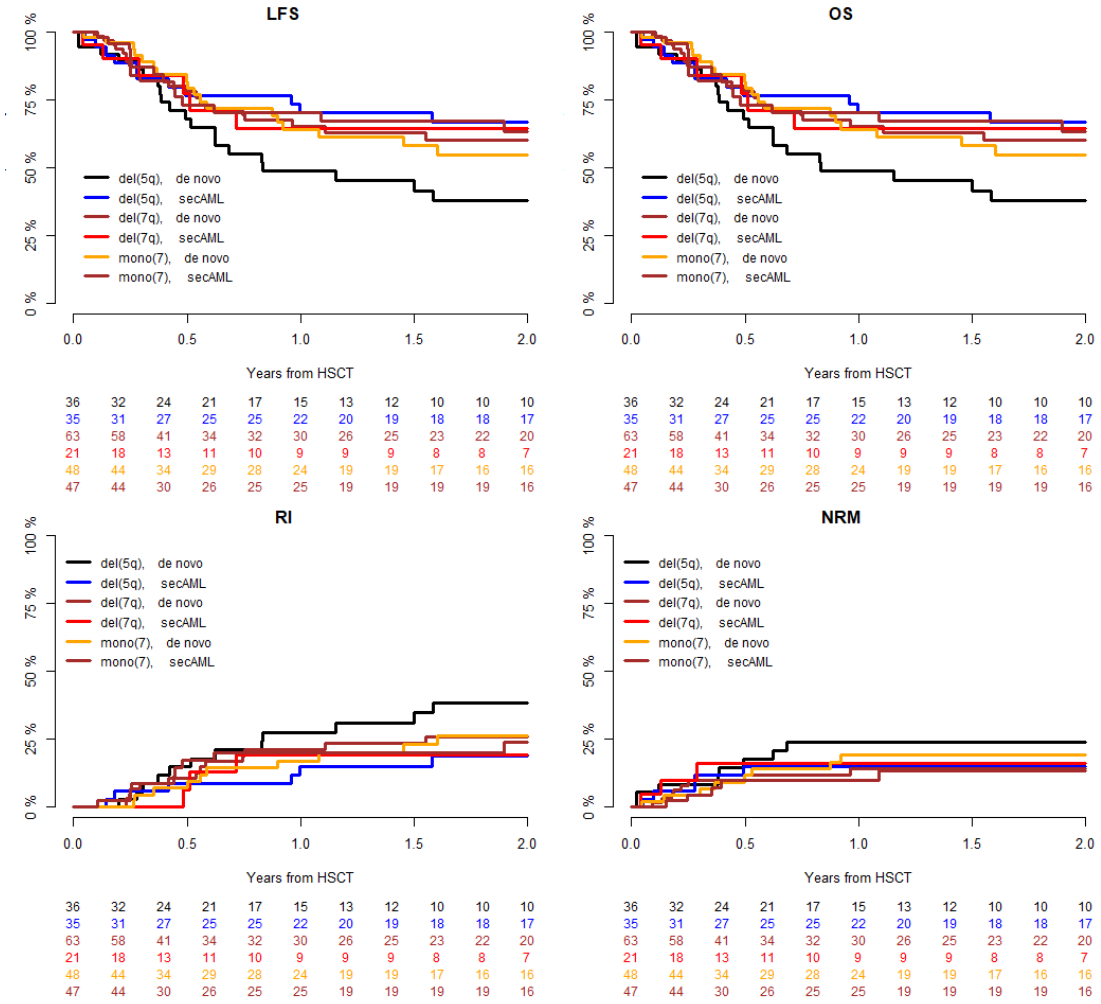

Table S1. Clinical outcomes by cytogenetic subgroup

Outcomes	All Estimation (95%CI)	del(7q) Estimation (95%CI)	mono(7) Estimation (95%CI)	del(5q) Estimation (95%CI)
Median FU, y	3 (2 - 3.6)	2.1 (1.3 - 3)	3 (1.9 - 4)	4.3 (3 - 5.1)
OS, 2 y (%)	64.9 (57.7 - 71.2)	68.7 (55.7 - 78.6)	61.5 (49 - 71.9)	65.3 (51.9 - 75.7)
LFS, 2 y (%)	57.5 (50.3 - 64)	61.3 (48.5 - 71.9)	58.6 (46.4 - 68.9)	52.3 (39.3 - 63.8)
RI, 2 y(%)	26 (20.1 - 32.3)	24.4 (14.6 - 35.5)	25.1 (15.8 - 35.6)	28.5 (17.8 - 40.1)
NRM, 2 y (%)	16.6 (12 - 21.8)	14.3 (7.5 - 23.2)	16.3 (9.1 - 25.3)	19.2 (10.8 - 29.5)
Poly recovery, 30 d (%)	93.1 (89 - 95.7)	93.9 (85.4 - 97.5)	92.5 (84.5 - 96.4)	92.9 (82.9 - 97.1)
Platelet recovery, 60 d (%)	91.7 (87.2 - 94.7)	93.5 (84.4 - 97.4)	88.5 (79.4 - 93.8)	93.8 (83.3 - 97.8)
aGVHD-II/IV, 100 d (%)	28.4 (22.8 - 34.3)	30.3 (20.7 - 40.5)	25.6 (17 - 34.9)	29.9 (19.4 - 41.1)
aGVHD-III/IV, 100 d (%)	8.4 (5.3 - 12.4)	9.7 (4.5 - 17.3)	6.7 (2.7 - 13.1)	9 (3.6 - 17.4)
cGVHD, 2 y (%)	33.7 (27 - 40.4)	42.9 (29.9 - 55.2)	35.5 (24.5 - 46.6)	22.1 (12.4 - 33.6)
cGVHD ext, 2 y (%)	13.4 (9.1 - 18.7)	14.6 (7.1 - 24.7)	19.4 (11.1 - 29.4)	5.2 (1.3 - 13.1)
GRFS, 2 y (%)	44.4 (37.4 - 51.2)	48.7 (36.2 - 60.1)	39.4 (28.1 - 50.5)	46.2 (33.5 - 57.9)

Abbreviations: CI: confidence interval; del: deletion; mono: monosomy; FU: follow-up; y: year; OS: overall survival; LFS: leukemia-free survival; RI: relapse incidence; NRM: non-relapse mortality; Poly: polymorphonuclear leukocytes d: day; y: year; GVHD: graft-versus-host disease; ext: extensive; GRFS: graft-versus-host disease-free, and relapse-free survival.

Table S2. Multivariate Analysis

		LFS		OS		RI		NRM	
Variables	**Modalities**	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Cytogenetic subgroup	**del(7q)**	1		1		1		1	
	mono(7)	1.05 (0.62-1.78)	0.86	1.13 (0.62-2.07)	0.68	1.07 (0.54-2.13)	0.85	1.05 (0.45-2.45)	0.91
	del(5q)	1.26 (0.74-2.16)	0.4	1.02 (0.54-1.93)	0.95	1.26 (0.63-2.55)	0.51	1.26 (0.53-2.99)	0.6
Type of AML	**de novo**	1		1		1		1	
	Sec AML	0.66 (0.41-1.05)	0.08	0.74 (0.44-1.25)	0.26	0.64 (0.35-1.18)	0.15	0.67 (0.32-1.41)	0.29
Donor type	**Matched related**	1		1		1		1	
	Mismatched related	0.97 (0.44-2.15)	0.94	1.1 (0.46-2.61)	0.84	0.62 (0.19-2)	0.43	1.6 (0.5-5.11)	0.43
	Unrelated	1.06 (0.62-1.81)	0.84	0.82 (0.45-1.51)	0.53	1.06 (0.53-2.11)	0.88	1.01 (0.42-2.45)	0.98
Myeloablative regimen	**No**	1		1		1		1	
	Yes	1.25 (0.78-2.02)	0.35	1.23 (0.71-2.14)	0.47	1.03 (0.54-1.94)	0.93	1.65 (0.78-3.48)	0.19
Age at HCT (effect for 10 y)		1.21 (1-1.48)	0.06	1.38 (1.09-1.75)	0.007	1.16 (0.9-1.51)	0.26	1.28 (0.93-1.76)	0.13
Year of HCT		1.01 (0.95-1.08)	0.74	0.99 (0.91-1.07)	0.72	1.03 (0.94-1.13)	0.52	0.98 (0.88-1.09)	0.75

Abbreviations: HR: hazard ratio; CI: confidence interval; del: deletion; mono: monosomy; OS: overall survival; LFS: leukemia-free survival; RI: relapse incidence; NRM: non-relapse mortality; AML: acute myeloid leukemia; sec: secondary; HCT: hematopoietic cell transplantation; y: year.