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Bone Marrow WT1 Levels in Allogeneic Hematopoietic Stem Cell Transplantation for Acute Myelogenous Leukemia and Myelodysplasia: Clinically Relevant Time Points and 100 Copies Threshold Value

Josep F. Nomdedéu [1,*], Albert Esquirol [2], Maite Carricondo [1], Marta Pratcorona [1], Montserrat Hoyos [1], Ana Garrido [2], Miguel Rubio [1], Elena Bussaglia [1], Irene García-Cadenas [2], Camino Estivill [1], Salut Brunet [2], Rodrigo Martino [2], Jorge Sierra [2]

[1] *Hematology Laboratory, IIB-Sant Pau and Jose Carreras Leukemia Research Institutes, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain*

[2] *Hematopoietic Transplant Program, Hematology Department, IIB-Sant Pau and Jose Carreras Leukemia Research Institutes, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain*

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The outcome of allogeneic hematopoietic stem cell transplantation (HCT) in patients with myeloid malignancies is better in those without minimal residual disease (MRD) than in those with MRD+, as assessed by multiparametric flow cytometry (MPFC). WT1 quantitation also has been used to assess the probability of relapse in acute myelogenous leukemia (AML) treated with chemotherapy. We analyzed the clinical value of normalized bone marrow WT1 levels as a measure of the expanded myeloid progenitor compartment in a consecutive series of 193 adult patients with myeloid malignancies who underwent HCT. Bone marrow WT1 levels before the HCT, at the first bone marrow aspirate after infusion, and in the follow-up samples after HCT were determined by means of real-time PCR using the European LeukemiaNet normalized method. We sought to clarify the prognostic relevance in terms of overall survival (OS), progression-free survival (PFS), and cumulative incidence of relapse (CIR). Based on earlier experience in AML, we selected a threshold of 100 copies, defining 2 groups: patients with <100 WT1 copies and those with ≥100 copies. Patients with <100 WT1 copies before HCT (median time, 36 days; range, 4 to 268 days) had a better OS, PFS, and CIR than those with ≥100 copies (40 ± 1 versus 29 ± 6 days, $P = .004$; 35 ± 9 versus 26 ± 6 days, $P = .002$; and 29 ± 7 versus 37 ± 6 days, $P = .051$). In the first bone marrow study after the HCT (median time, 42 days; range 14 to 157 days, respectively), patients with <100 WT1 copies also had better outcomes in terms of OS, PFS, and CIR (40 ± 7 versus 31 ± 9 days, $P = .025$; 36 ± 7 versus 30 ± 8 days, $P = .004$; and 29 ± 6 days versus 54 ± 9, $P < .001$, respectively). At this time point, bone marrrow samples with >100 copies also included patients who were negative for MRD as assessed by MPFC (19 of 32). During the HCT follow-up, patients with sustained WT1 levels <100 copies showed a marked benefit in terms of OS, PFS, and CIR even compared with those with only a single measurement >100 copies (mean, 68 ± 11 versus 26 ± 7 days, $P < .001$; 63 ± 11 versus 20 ± 8 days, $P < .001$; and 20 ± 8 vs. 71 ± 8 days, $P < .001$, respectively). Standardized bone marrow WT1 levels using a 100-copy threshold in samples obtained before HCT, at leukocyte recovery, and during follow-up provided relevant prognostic information in patients with myeloid malignacies submitted to HCT.

INTRODUCTION

The analysis of minimal residual disease (MRD) at different time points provides useful information in patients with myeloid malignancies who have undergone allogeneic hematopoietic stem cell transplantation (HCT). Patients with negative MRD respond much better that those with MRD+ [1-4]. Given that a high number of patients with acue myelogenous leukemia (AML) lack specific chimeric rearrangements that can be monitored by sensitive PCR

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* Correspondence and reprint requests: Josep F. Nomdedéu, MD, Laboratori d'Hematologia, Servei d'Hematologia, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Mas Casanovas, 90, Barcelona, 08041, Spain.

E-mail address: jnomdedeu@santpau.cat (J.F. Nomdedéu).

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methods, most studies have been performed using multiparametric flow cytometry (MPFC), which relies on the identification of aberrant immunophenotypes [5]. The advent of more robust and more sensitive sequencing platforms and the use of digital PCR will enable direct analysis of driver mutations in myeloid malignancies. Some such mutations can be detected in the bone marrow in morphological complete remission (CR), however [6].

In earlier studies, we analyzed the value of WT1 expression in risk assessment in patients with AML, and found that normalized bone marrow WT1 levels provide useful information on risk stratification [7]. WT1 is a transcription factor that is overexpressed in granulocyte-monocyte precursors and down-regulated as the myeloid cells differentiate [8-10]. Based on its expression in a subset of bone marrow $CD34^+$ cells and its up-regulation in most patients with AML and myelodysplastic syndrome (MDS), overexpression of WT1 is a surrogate marker of abnormal myelopoiesis and has been used as a relapse risk stratification tool in myeloid malignancies [7,11-18]. WT1 in bone marrow identifies hematopoiesis enriched in leukemic cells, as shown by frequent leukemia relapses in AML patients autografted with mobilized peripheral blood hematopoietic cells harboring high WT1 levels [18].

Despite efforts to standardize WT1 bone marrow levels, some authors have pointed out that WT1 mRNA quantitation is not sufficiently sensitive for use as a reliable marker of MRD. It is also argued that the WT1 thresholds are within the same range as those in normal bone marrow. In sharp contrast with MPFC, which is also a surrogate marker of cells harboring driver mutations, WT1 is not widely recognized as a "prime time" MRD tool.

Despite their biological limitations, bone marrow WT1 levels as a marker of bone marrow with an enlarged immature compartment could become an almost universal target for assessing the quality of remission achieved in myeloid malignancies. Their expression in AML and MDS is up-regulated in parallel with the immature cell number. In this respect, some authors have also recently used WT1 levels to predict relapse in bone marrow transplant recipients [19-25]. Given that lack of consensus on clinically relevant WT1 thresholds and time points in the HCT setting to guide clinical decisions (eg, immunosupressive withdrawal, donor lymphocyte infusion, chemotherapy, hypomethylating agents), WT1 quantitation has not yet gained widespread use.

To investigate the prognostic impact of normalized bone marrow WT1 levels in adult patients with AML and MDS, we retrospectively analyzed a consecutive series of patients who underwent HCT at Hospital de la Santa Creu i Sant Pau in Barcelona. We assessed whether WT1 levels can be useful in predicting outcomes in this group of patients.

PATIENTS AND METHODS

A total of 1031 bone marrow samples were collected from 193 patients at different time points: (1) before the hematopoietic stem cell infusion (177 samples), (2) at the first bone marrow aspirate (184 samples) after HCT, and (3) during the post-HCT follow-up (670 samples) Diagnostic samples from all patients were analyzed for mutations in the *NPM1*, *FLT3*, *CEBPA*, *MLL*, and *WT1* genes using well-established protocols [7,26,27]. Patient characteristics are summarized in Table 1. Mononuclear cells were separated using Lymphoprep (Axis-Shield, Oslo, Norway) and lysed with Trizol reagent (Invitrogen, Thermo Fisher Scientific, Waltham, MA) according to the manufacturer's instructions. Then 1 μg of RNA was reverse-transcribed to cDNA in a total reaction volume of 20 μL containing 5 mM Cl_2Mg, 10× buffer, 10 mM DTT, 10 mM each dNTPs, 15 μM of random hexamers, 20 U of RNAsin (Promega, Madison, WI) and 200 U of MMLV enzyme (Applied Biosystems, Foster City, CA). Samples were incubated for 10 minutes at 20°C, 45 minutes at 42°C, and 3 minutes at 99°C, followed by 10 minutes at 4°C. WT1 expression levels were determined by real-time quantitative PCR (qRT-PCR) in an ABI PRISM 7500 Genetic Analyzer (Applied Biosystems) using the primers and conditions described by the European LeukemiaNet (ELN) group [11]. For WT1 copy number titration, we used Ipsogen plasmid (Qiagen, Marseilles, France). The WT1 gene transcripts obtained by qRT-PCR were normalized with respect to the number of *ABL* transcripts and expressed as copy numbers per 10^4 copies of *ABL*.

All samples were performed in triplicate, and those with inferior RNA quality or a threshold cycle number exceeding 30 were excluded from our analyses. Results are expressed as copies, and 25 normal bone marrow samples were used as test controls [11,13].

Table 1
Patient Characteristics

Characteristic	Value
Number of cases	193
Male sex, n (%)	111 (57.5)
Female donor to male recipient, n (%)	46 (23.8)
Age, yr, median (range)	49 (17-70)
Age ≥30 yr, n (%)	22 (11.4)
Age 31-50 yr, n (%)	68 (35.2)
Age >50 yr, n (%)	103 (53.4)
Response, n (%)	
Complete remission (first or second)	130 (67.4)
Other responses	63 (32.6)
rDRI, n (%)	
Low	7 (3.6)
Intermediate	109 (56.5)
High	62 (32.1)
Very high	15 (7.8)
AML, n (%)	148 (76.7)
MDS, n (%)	45 (23.3)
Donor, n (%)	
Identical sibling	103 (53.4)
Other donors	90 (46.6)
Conditioning regimen, n (%)	
Myeloablative	79 (40.9)
Reduced-intensity	98 (50.8)
Sequential regimen	16 (8.3)
Graft-versus-host disease prophylaxis, n (%)	
Cyclosporine-MTX or MMF	134 (69.4)
Sirolimus-tacrolimus	26 (13.5)
Cyclosporine-prednisone	25 (13)
Other	8 (4.1)
Stem cell source, n (%)	
Peripheral blood	162 (83.9)
Bone marrow	29 (15)
Cord blood	2 (1)
Follow-up of survivors, yr, median (range)	4.4 (0.6-11.5)

MMF indicates mycophenolate mofetil; MTX, methotrexate.

IMMUNOPHENOTYPING

To assess aberrant immunophenotypes by MPFC, we used combinations of 3 or 4 antigens as described elsewhere. We acquired 10,000 ungated events in a first step, and based on the reactivity of CD34, CD45, CD33, CD117, CD123, and CD15 markers, an additional 200,000 events were processed to detect leukemia-associated immunophenotypes [26,27] to reach a sensitivity of 10^{-4}. Aberrant immunophenotypes were identified by a single observer (J.N.) and are reported as a percentage.

HCT REGIMENS

Patients were treated between 2004 and 2011 according to the CETLAM AML-03 protocol trial [26]. Informed consent was obtained from each patient. Adults up to 70 years of age received induction chemotherapy with idarubicin, intermediate-dose cytarabine, and etoposide, followed by consolidation with mitoxantrone and intermediate-dose ara-C (cytarabine). G-CSF priming during induction and

consolidation was administered together with the chemotherapy. Patients with favorable cytogenetics at diagnosis then received 1 cycle of high-dose cytarabine. Those with a normal karytotype and needing a single course to achieve CR were treated with autologous HCT. Patients with favorable cytogenetics and high leukocyte counts at diagnosis were also treated with autologous transplantation instead of high-dose cytarabine. A favorable genotype was defined as the presence of *NPM1* or biallelic *CEBPA* mutations associated without *FLT3* internal tandem duplication (FLT3-ITD). Patients with a normal karyotype but adverse molecular profile (FLT3-ITD or MLL rearrangements, including partial tandem duplication assessed by long-distance PCR) were allocated to the treatment for unfavorable cases; these included HCT from an HLA-identical donor (related or unrelated) or autologous transplant after "in vivo" purging with 3 mg/m^2 i.v. of Mylotarg. Cases with MDS were referred to HCT in accordance with institutional protocols that take into account the International Prognostic Scoring System. Patients age ≥50 years with an allogeneic donor received reduced-intensity conditioning with fludarabine and busulfan.

STATISTICAL METHODS

Overall survival (OS) was measured from the date of enrollment until the date of death. Progression-free survival (PFS) was defined as the interval from day 0 to disease progression or death. OS and PFS were plotted using the Kaplan–Meier method; differences between curves were analyzed by the log-rank test. The cumulative incidence estimates with competing risks were used to calculate the incidences of relapse and nonrelapse mortality (NRM). The competing risk for NRM was relapse, and the competing risk for relapse was NRM. After exploratory univariate comparisons, multivariate analyses were performed, including the variables with a $P < .15$. COX regression analyses was used for multivariate analyses. A landmark analysis was done for survivors after 180 days, excluding those patients who had died or relapsed before that date. PFS was compared between patients who had a WT1 determination between 180 and 365 days. Threshold values were established by selecting the most accurate values using a nonparametric receiver operating characteristic (ROC) curve analysis, taking into account the maximum sensitivity-specificity ratio. The endpoints for the threshold were relapse and death. This approach was applied following the REMARK guidelines [28].

The statistical packages used were the SPSS 19.0.0 (IBM, Armonk, NY), the open- source integrated development environment (IDE) GNU Emacs 23.4.1, RStudio version 0.94–110 (RStudio, Boston, MA), and R version 2.14.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

HCT outcomes are shown in Tables 2 and 3. One hundred and eleven patients (57.5%) were male. The median age at HCT was 49 years (range, 17 to 70 years). One hundred and forty-eight patients (76.7%) had AML, and 45 patients (23.3%) had MDS. One hundred and thirty patients (67.4%) were in first or second CR at HCT. Patients' refined Disease Risk Index (rDRI) score was low in 3.6% of cases, intermediate in 56.5%, high in 32.1%, and very high in the remaining 7.8%. Seventy-nine patients (40.9%) received a myeloablative conditioning regimen. An identical sibling donor was used in 103 patients (53.4%) and the most common stem cell source was peripheral blood (162 patients; 83.9%).

Table 2
Hematopoietic Reconstitution and WT1 Determination

Variable	Value
Achieved stable neutrophils >0.5 × 10^9/L	
Day of neutrophils > 0.5 × 10^9/L, median (range)	18 (10-38)
Cumulative incidence (95% CI) of neutrophil recovery at day +30, %	95.3 (92.3-98.3)
Graft failure: primary, n (%)	3 (1.6)
Achieved stable platelet count >20 × 10^9/L	
Day of platelets >20 × 10^9/L, median (range)	17 (6-78)
Cumulative incidence (95% CI) of platelet recovery to >20 × 10^9/L at day +60, %	92 (88.4-96)
Cumulative incidence of acute grade II-III GVHD	
Cumulative incidence (95% CI) of acute grade II-IV GVHD at day +100, %	26.4 (20-33)
Day of onset, median (range)	45 (13-100)
Cumulative incidence (95% CI) of acute grade II-IV GVHD at day +365, %	33.12 (24.5-38)
Cumulative incidence of chronic GVHD	
Cumulative incidence (95% CI) of limited chronic GVHD	38.5 (34-42)
Cumulative incidence (95% CI) of extensive chronic GVHD	20 (18-22)
Pre-HCT WT-1 determination	
<100 copies, n (%)	107 (60.5)
≥100 copies, n (%)	70 (39.5)
Time of determination, d, median (range)	36 (4-268)
Post-HCT WT-1 determination	
<100 copies, n (%)	152 (82.6)
≥100 copies, n (%)	32 (17.4)
Time of determination, d, median (range)	42 (14-157)
Pre-HCT WT-1 determination ≥100 copies, n	70
Complete morphological CR, n	
Negative MRD by flow cytometry:	12
Positive MRD by flow cytometry:	20
Other active disease, n	38
Post-HCT WT-1 determination ≥100 copies, n	32
Positive MRD by flow cytometry and/or morphology, n	
Relapsed	11
Not relapsed	2
Negative MRD by flow cytometry, n	
Relapsed	7
Not relapsed	12 (6 developed GVHD)

CI indicates confidence interval; GVHD, graft-versus-host disease.

BONE MARROW WT1 LEVELS BEFORE HCT

A bone marrow RNA sample to perform WT1 quantitation before HCT was available in 177 patients (91.7%) (median time, 36 days; range, 4 to 268 days). Patients with <100 WT1 copies had better OS, better PFS, and lower CIR than those with ≥100 WT1 copies (Figure 1). The 70 patients with ≥100 WT1 copies in bone marrow were divided into 3 groups. In 38 patients, blasts were observed at microscopic examination (not in CR). In 20 patients, the morphology showed no blasts but MPFC was MRD+ (MRD ranging from 0.07% to 2.8%). In 12 patients, both morphology and MPFC were negative, and an elevated WT1 level was the sole sign of a poor-quality remission (12 of 32 patients in CR had WT1 levels >100 copies and negative MPFC). Four of these 12 patients relapsed and died. Four other patients from this group died as a consequence of a competitive event, including infection in 2 patients and severe and refractory acute graft-versus-host disease in the other 2. Only 4 patients were alive at study end, 3 of whom

Table 3
Allogeneic HCT Outcomes

Outcome	Value
OS probability (95% CI), %	
At 1 yr	59.8 (56-63)
At 4 yr	46 (42-50)
At 12 yr	37.6 (32-43)
PFS probability (95% CI), %	
At 1 yr	54.6 (51-58)
At 4 yr	43.5 (40-47)
At 12 yr	33.2 (27-39)
NRM, cumulative incidence (95% CI), %	
At 100 d	11.3 (7-16)
At 1 yr	23.5 (18-30)
At 4 yr	30.7 (22-35)
At 12 yr	36.2 (23-39)
Disease progression or relapse, cumulative incidence (95% CI), %	
At 100 d	12.4 (8-17)
At 1 yr	22.4 (16-28)
At 4 yr	26.3 (16-28)
At 12 yr	31.2 (20-33)

had no therapeutic intervention other than HCT. In the fourth patient, a mixed chimerism was identified in the post-HCT phase. The attending physician decided to discontinue the immunosuppressive treatment and the patient again achieved CR.

BONE MARROW WT1 LEVELS IN THE FIRST EVALUATION ASPIRATE AFTER HCT

WT1 level quantitation after hematopoietic cell infusion was obtained in 184 patients (median time, 42 days, range, 14 to 157 days). Again, the 100-copy threshold clearly distinguished 2 groups in terms of OS, PFS, and CIR (Figure 2). In the group with WT1 levels exceeding 100 copies (32 patients), we also found 3 categories: 11 patients not in morphologic CR, 2 patients without blast cells by morphology with a positive MRD by MPFC (MRD 0.07% and 0.3%, respectively), and 19 patients with >100 WT1 copies, no blasts by morphology (CR), and negative MRD by MPFC (Table 2).

CLINICAL RELEVANCE OF SUSTAINED WT1 LEVELS <100 COPIES AFTER HCT

Post-HCT WT1 levels were available from 670 samples. Patients were categorized into two groups: those showing sustained levels <100 copies (3 or more samples with levels always below the 100-copy threshold; n = 56) and those with 3 or more samples available after HCT and showing bone marrow WT1 levels >100 copies (n = 48) in at least one determination. Using these criteria, we identified marked differences in terms of OS, PFS, and CIR (Figure 3). These findings suggest that at any time after HCT, the appearance of bone marrow WT1 levels >100 copies is associated with a very high probability of relapse and death (Table 2) (Supplementary Material).

MULTIVARIATE ANALYSIS REVEALED AN INDEPENDENT PROGNOSTIC VALUE OF BONE MARROW WT1 LEVELS POST-HCT

Univariate analysis performed at 4 years (median follow-up for survivors) disclosed statistically significant associations between OS, PFS, and CIR with status at HCT (first CR versus other), Disease Risk Index (DRI; categorized as low to intermediate versus high to very high), GVHD prophylaxis (sirolimus-tacrolimus versus other), female donor to male recipient, and pre-HCT and post-HCT WT1 levels (Supplementary Materials). Multivariate analysis showed the prognostic impact of bone marrow WT1 levels (Table 4).

DISCUSSION

Our data show that in patients with AML and MDS, bone marrow WT1 levels before HCT and at the first bone marrow examination after HCT were predictive of OS, PFS, and CIR. Furthermore, patients with sustained levels of bone marrow WT1 <100 copies after HCT had excellent outcomes. Interestingly, bone marrow aspirates with elevated WT1 levels at any time point, irrespective of the results from conventional morphology or MPFC, may identify patients with a high probability of relapse. The probabilities of relapse and death were higher in patients with >100 bone marrow WT1 copies at each time point measured (Figures 1, 2 and 3). These findings suggest that suboptimal remission status in myeloid malignancies can be detected not only by morphology or by MPFC, but also by WT1 mRNA quantitation using the ELN method. Remarkably, some patients with >100 WT1 copies were free of blasts by morphology and/or flow cytometry. Other patients with high WT1 levels had detectable leukemia by morphological examination and/or MPFC [22,23]. This phenomenon was observed pre- and post-HCT. In the latter group, it may be argued that the scarce bone marrow cellularity frequently obtained early after transplantation (only 200,000 events for each tube acquired in our study) makes the sensitivity of MPFC suboptimal.

As hypothesized by other groups, normal bone marrow WT1 levels or, more precisely, those associated with a low probability of myeloid malignancy relapse, are not in the same range of normal bone marrow and could be similar to those observed in normal peripheral blood or those associated with successful chemotherapy induction in AML [29,30]. Our findings require confirmation in other series, especially regarding the clinical relevance of the selected time points. Such confirmation could reinforce post-HCT interventions, such as hypomethylating agents, targeted therapies, and immune approaches based on persistent high WT1 levels. The bone marrow threshold used in this study was the same as that described by Pozzi et al. [19] in their patients who underwent HCT. As we pointed out in a previous study in adults with AML [7], our present findings should be confirmed with other standardized methods of WT1 quantitation [31]. Whether our findings also apply to pediatric patients should be explored as well [32,33]. In this regard, an elevated WT1 level before HCT was identified as an adverse prognostic factor in children with hematologic malignancies.

The 2 most commonly used techniques to assess MRD status are MPFC and qRT-PCR. Some allografted patients have been followed using both MPFC and WT1 quantitation [20,21]. This combined approach has shown improved relapse prediction. Other authors have used the combination of WT1 quantitation with chimerism analysis [23].

In some reports, peripheral blood has been used to assess WT1 levels. This can make follow-up of patients with HCT easier. Using this sample source, Israyelyan et al. [34] reported 50 copies as the threshold for predicting relapse in HCT recipients with AML and MDS. Recently, circulating RNA in peripheral blood was also used as relapse prediction marker in HCT recipients [24]. Dulery et al. [35] reported the value of WT1 quantitation in predicting relapse in the HCT setting; they used the same WT1 test (Ipsogen) in peripheral blood samples obtained in the post-HCT phase and identified the 3-month time point as the most useful. In a series of patients

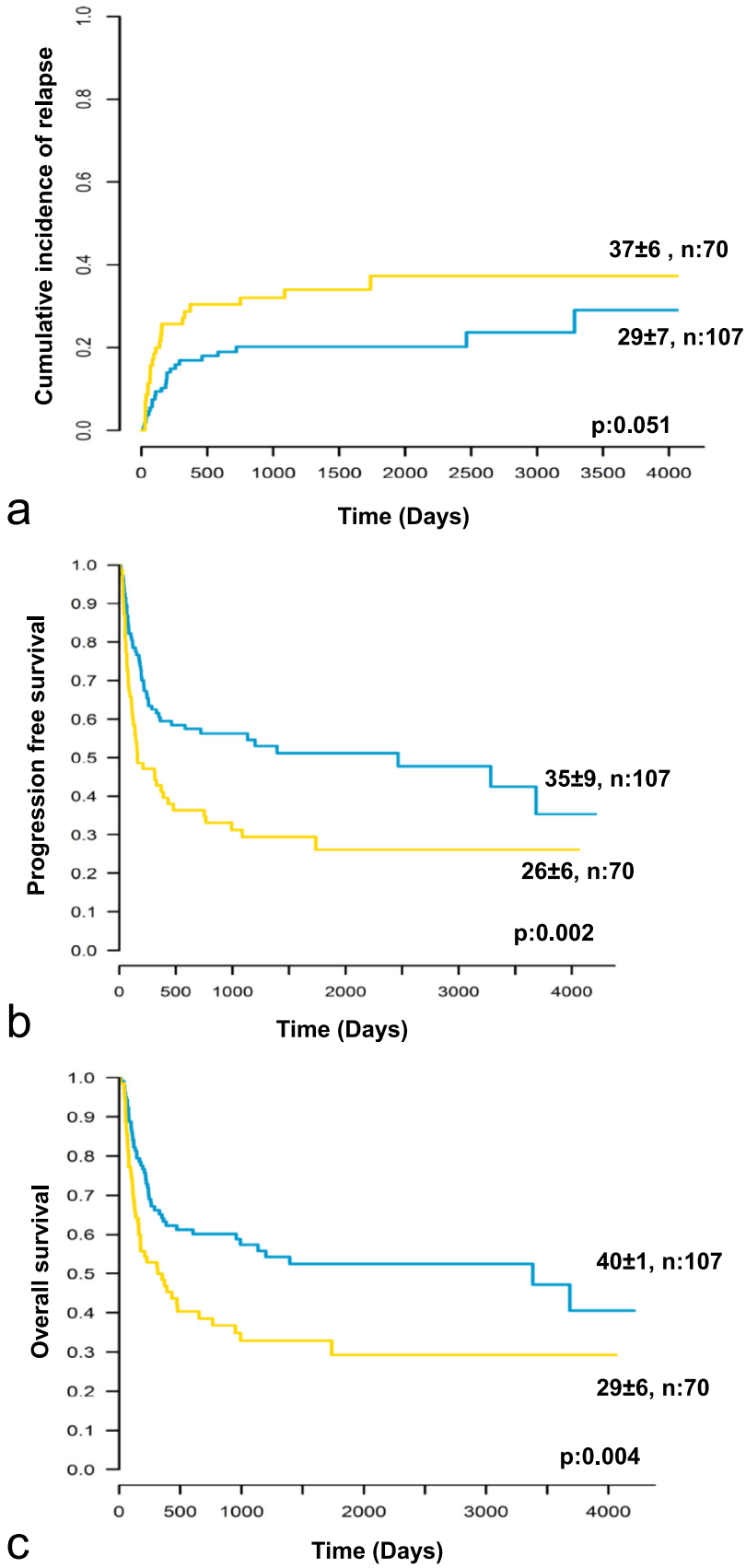

Figure 1. Bone marrow WT1 levels before HCT identified 2 relevant groups based on a WT1 threshold of 100 copies: high WT1 (orange curves) and low WT1 (blue curves). Shown are the CIR (A), PFS (B), and OS (C), in days.

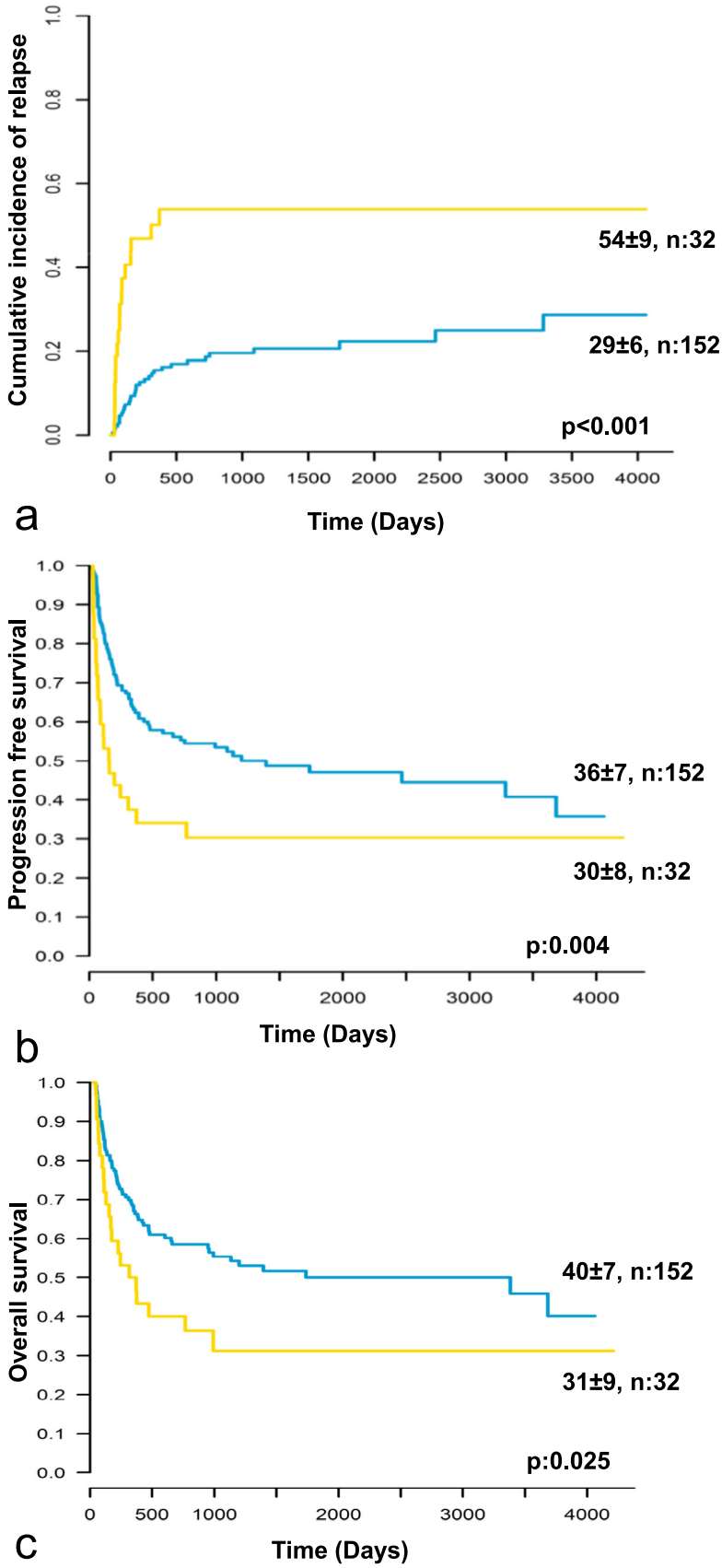

Figure 2. Bone marrow WT1 levels at the first bone marrow aspirate after HCT. A 100-copy threshold identified 2 relevant groups: high WT1 (orange curves) and low WT1 (blue curves). Shown are CIR (A), PFS (B), and OS (C), in days.

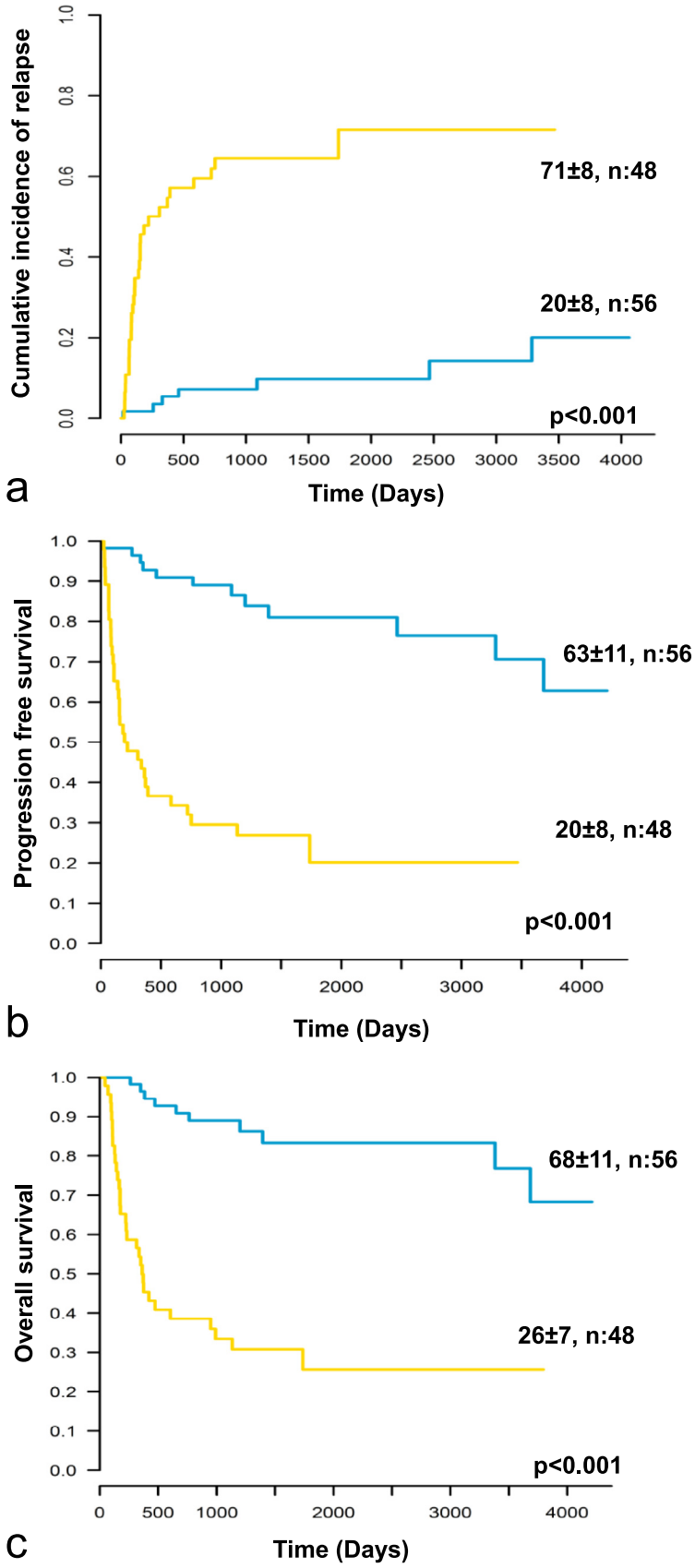

Figure 3. Bone marrow WT1 levels after HCT: relevance of the sustained levels below 100 copies. Shown are the CIR (A), PFS (B), and OS (C), in days. High WT1 is represented by orange curves; low WT1, by blue curves.

Table 4
Multivariate Analysis at 4 Years: OS, PFS, NRM, and Disease Relapse

Outcome	Variable	*P* Value	HR	95% CI
OS	Status at HCT: first CR versus other response	.001	0.34	0.21-0.53
	GVHD prophylaxis: sirolimus-tacrolimus versus other response	.015	0.35	0.15-0.81
	Female-to-male donor direction versus other	.001	2.41	10.52-30.83
	<100 WT1 copies versus >100 copies after HCT	.035	0.57	0.34-0.96
PFS	Status at HCT: first CR versus other response	.001	0.37	0.23-0.57
	GVHD prophylaxis: sirolimus-tacrolimus versus other response	.007	0.31	0.13-0.73
	Female-to-male donor direction versus other	.001	2.11	10.34-30.33
	<100 WT1 copies versus >100 copies after HCT	.002	0.450	0.27-0.73
Relapse	GVHD prophylaxis: sirolimus-tacrolimus versus other response	.029	0.20	0.04-0.85
	WT1 <100 copies versus >100 copies pre-HCT	.007	0.42	0.22 – 0.79
	WT1 <100 copies versus >100 copies post-HCT	.001	0.19	0.10 – 0.37
NRM	Status at HCT: first CR versus other response	.001	0.29	0.15 – 0.55
	Female-to-male donor direction versus other	.002	2.62	1.44 – 4.79

HR indicates hazard ratio.

with AML treated with HCT, Rossi et al. [36] observed that WT1 quantitation was most predictive at 3 months post-HCT, whereas MPFC was most useful before HCT and at day 30 post-HCT. Here we have shown that late bone marrow WT1 determinations are also useful, given that those patients who were below the 100-copy threshold had good outcomes. Di Grazia et al. [25] reported the benefits of starting preemptive immunotherapy, and, in accordance with our results, their optimal threshold was also 100 copies. Yoon et al. [37] used the same test to analyze a series of 82 patients with MDS, and found similar thresholds predictive of relapse. In another study, the same group found that this approach was also useful for predicting relapses in patients with AML with *NPM1* and *FLT3* mutations [38].

In conclusion, elevated pre-HCT and post-HCT WT1 levels are useful markers for predicting main outcomes in adults with AML and MDS treated with HCT. Prospective studies are needed to assess whether bone marrow WT1 levels >100 copies may be an indication to start treatments in the post-HCT phase. Patients with sustained low WT1 levels post-HCT (<100 copies) have excellent outcomes. Bone marrow WT1 quantitation using the ELN method is an easy-to-use tool for assessing remission in patients who have undergone HCT for AML or MDS.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at doi:10.1016/j.bbmt.2017.09.001.

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