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# The changing scene of allogeneic stem cell transplantation for chronic myeloid leukemia—a report from the German Registry covering the period from 1998 to 2004

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**Abstract** Due to the recent changes in the indication to allogeneic stem cell transplantation (SCT) in chronic myeloid leukemia (CML), we retrospectively analyzed 1,716 patients with different CML stages who received an allograft from related ( $n=767$ ) or unrelated donors ( $n=938$ ) within the German Registry of Stem Cell Transplantation (DRST) from 1998 to 2004. Myeloablative conditioning was performed in 724/871 cases (83%), dose-reduced conditioning in 147/871 (17%). Annual transplantations were decreasing from 357 to 98 (28%) in the period of study, but the proportion of advanced cases was increasing from 32% (112/346) to 53% (50/94) of all SCTs. Stage of

disease, intervals from diagnosis, and patients' age were independent prognostic parameters, while peripheral stem cells and unrelated transplantation seemed equal to bone marrow/related transplantation. This study demonstrates that allo-SCT still has an important role in advanced CML, which emphasizes the need for optimized transplantation strategies for these high-risk patients.

**Keywords** Allogeneic stem cell transplantation (SCT) · Chronic myeloid leukemia (CML) · Dose-reduced conditioning (RIC) · Myeloablative conditioning · German Registry of Stem Cell Transplantation (DRST)

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## Introduction

Indication to allogeneic stem cell transplantation (SCT) in chronic myeloid leukemia (CML) has experienced significant changes in recent years. After the introduction of the tyrosine kinase inhibitor (TKI) imatinib (IM) with estimated survival rates close to 90% after 5 years [1] and progression-free survival of >97% once major molecular remission is achieved [2], the annual transplantation rates in CML are worldwide decreasing [3, 4], especially since 2002, when IM was approved [5]. Treatment options are further broadened by second-generation TKIs such as nilotinib or dasatinib [6].

However, according to the recommendations of the European LeukemiaNet (ELN), allo-SCT should still be discussed in those patients who show failure of IM or suboptimal response [7]. Another first-line indication to allo-SCT is still represented by advanced disease such as accelerated (AP) or blast phase (BP). Due to the introduction of IM and of second-generation TKIs in the treatment before SCT [8, 9], more patients in advanced disease achieve remission before SCT [7, 10]. Therefore, allo-SCT took a shift towards advanced disease or cases with imatinib resistance [11, 12]. Reduced intensity conditioning (RIC) broadened transplantation strategies [13] and allowed the inclusion of patients with comorbidity, advanced disease, or higher age [14], who would have been excluded from SCT in former years.

With regard to the recent modifications of treatment strategies in CML, we here performed a retrospective multicenter analysis of all 1,716 adult and pediatric stem cell recipients with diverse stages of CML who had been registered within the German Registry of Stem Cell Transplantation (Deutsches Register für Stammzelltransplantation; DRST) in the period from 1998 to 2004. The aim of the study was to document changes of transplantation activity and of risk profiles of CML patients and to define outcomes and risk factors of current allo-SCT in these patients within the DRST.

## Patients and methods

From January 1998 to December 2004, a total of 1,716 patients receiving an allograft from unrelated or related donors were registered within the DRST by 30 transplantation centers and were included in this retrospective analysis. The minimum essential data set was available for 1,526 patients. For 45 patients, the current vital status was unknown. The maximum number of patients for time to event analyses was 1,671.

## Characteristics of patients and donors

There were 1,014 males (59.1%) and 701 females (40.9%) (sex missing in one case). Median age of patients was 40 years (range 1–68 years). Considering the distribution of patients within the diverse age groups, only 66 patients (4%) were >59 years of age, whereas the majority (1,528/1,716; 89%) was between 20 and 59 years old. Thus, most patients were in the age groups >40 years (53%) (Tables 1 and 2). The majority of patients in whom the stage of disease at SCT was available were in first chronic phase (1. CP) (1,084/1,626; 67%) while 542 (33%) were in more advanced disease. Transplantation was performed in 856 of 1,716 cases (50%) within the first year from diagnosis. The

**Table 1** Characteristics of all 1,716 patients and donors

Parameter	Number (%)
Patient's age	
<40 years	803/1,716 (46.8)
>40 years	913/1,716 (53.2)
Sex	
Males	1,014/1,715 (59.1)
Females	701/1,715 (40.9)
Unknown	1
Interval from diagnosis to SCT	
<1 year to SCT	860/1,716 (50.1)
>1 year to SCT	856/1,716 (49.9)
Disease status at transplantation	
CP1	1,084/1,626 (66.7)
CP2, CP3	203/1,626 (12.4)
AP	211/1,626 (13.0)
BP	128/1,626 (7.9)
Unknown	90
Donor type	
Matched sibling	616/1,705 (36.1)
Matched related	67/1,705 (3.9)
Matched unrelated	764/1,705 (44.8)
Mismatched related	90/1,705 (5.3)
Mismatched unrelated	168/1,705 (9.9)
Unknown	11
Donor–patient sex matching	
Fem. donor/male patient	306/1,565 (19.6%)
All others	1,259/1,565 (80.4%)
Unknown	151
Stem cell source	
PBSC	1,069/1,709 (62.6)
BM	640/1,709 (37.4)
Unknown	7

**Table 2** Five years overall survival (OS) of patients with CML, univariate analysis

Parameter	All patients		<i>p</i>
	Number	5-year OS	
<b>Patients' sex</b>			
Male	683/1,671	55% (95% CI=52–56)	0.05
Female	988/1,671	62% (95% CI=58–66)	
<b>Patient's age</b>			
1–19	119/1,671	47% (95% CI=37–57)	<0.001
20–39	661/1,671	67% (95% CI=63–71)	
40–59	829/1,671	54% (95% CI=50–58)	
>59	62/1,671	37% (95% CI=17–57)	
<40 years	780/1,671	64% (95% CI=60–68)	
≥40 years	891/1,671	53% (95% CI=49–57)	
<b>Status of remission</b>			
CP1	1,058/1,587	70% (95% CI=67–73)	<0.001
Others	529/1,587	34% (95% CI=29–39)	
Unknown		84	
<b>Interval from diagnosis to SCT</b>			
≤1 year	838/1,671	66% (95% CI=62–70)	<0.001
>1 year	833/1,671	50% (95% CI=46–54)	
<b>Type of donor</b>			
Unrelated	914/1,662	55% (95% CI=51–59)	0.004
Related	748/1,662	61% (95% CI=57–65)	
Unknown		9	
<b>Donor sex</b>			
Male	917/1,526	58% (95% CI=54–62)	0.29
Female	609/1,526	55% (95% CI=51–56)	
Unknown		145	
<b>Donor–patient sex matching</b>			
Fem. donor/male patient	301/1,526	49% (95% CI=43–55)	0.004
All others	1,225/1,526	59% (95% CI=56–62)	
Unknown		145	
<b>HLA compatibility</b>			
HLA match	1,407/1,662	60% (95% CI=57–63)	<0.001
HLA mismatch	255/1,662	45% (95% CI=38–52)	
Unknown		9	
<b>Source of stem cells</b>			
BM	626/1,665	64% (95% CI=60–68)	0.004
PBSC	1,039/1,665	54% (95% CI=50–58)	
Unknown		6	
<b>Conditioning</b>			
RIC	147/871	42% (95% CI=33–51)	<0.001
Standard	724/871	62% (95% CI=58–66)	
Unknown		800	
<b>TBI</b>			
With TBI	823/1,646	58% (95% CI=54–62)	0.076
Without TBI	823/1,646	56% (95% CI=52–60)	
Unknown		25	
<b>Gratwohl score</b>			
0–1	142/1,162	71% (95% CI=62–80)	<0.001
2	246/1,162	78% (95% CI=72–84)	

**Table 2** (continued)

Parameter	All patients		<i>p</i>
	Number	5-year OS	
3	312/1,162	64% (95% CI=58–70)	
4	242/1,162	48% (95% CI=40–56)	
5–7	220/1,162	32% (95% CI=25–39)	
Unknown		186	
Year of SCT			
1998 (2–3–5 years)	356/1,671	62–60–58% (95% CI=57–67; 55–65; 53–64)	0.16
1999 (2–3–5 years)	367/1,671	59–54–52% (95% CI=54–65; 48–60; 46–58)	
2000 (2–3–5 years)	253/1,671	63–61–61% (95% CI=57–69; 55–67; 55–67)	
2001 (2–3–5 years)	239/1,671	63–60–57% (95% CI=57–70; 53–67; 49–65)	
2002 (2–3 years)	236/1,671	62–60% (95% CI=55–69; 68–53)	
2003 (2 years)	126/1,671	64% (95% CI=54–74)	
2004 (1 year)	94/1,671	76% (95% CI=65–87)	

OS overall survival; CPI first chronic phase; AP accelerated phase; BP blast phase; SCT allogeneic stem cell transplantation; BM bone marrow; PBSC peripheral blood stem cells; RIC reduced intensity conditioning; TBI total body irradiation

majority of SCTs was performed from unrelated donors (932/1,705 patients; 55%); 773/1,705 recipients had a related donor (45%), of these in eight cases a twin. HLA-matched donors were available for 1,447/1,705 stem cell recipients (85%). The majority of SCTs was sex matched (936/1,565; 60%). Donors were female in 624/1,566 cases (40%) and male in 942/1,566 cases (60%) where data were available. Peripheral blood stem cells (PBSC) (1,069/1,709; 63%) were more frequently used as stem cell source than bone marrow (BM) (640/1,709; 37%). No patient received cord blood.

Conditioning was performed by dose-reduced strategies (RIC) in 156/903 patients (17%) and by standard conditioning (SIC) in 747/903 patients (83%) (conditioning strategies were available only in part of registered patients). Total body irradiation (TBI) was included in the conditioning regimens in 842/1,688 patients (50%).

Standard conditioning was either based on busulfan (cumulative dosage 12 mg/m<sup>2</sup>) combined with cyclophosphamide (cum. 120 mg/m<sup>2</sup>) or on TBI-based protocols (cum. 12 Gy) in combination with cyclophosphamide (cum. 120 mg/m<sup>2</sup>). Reduced conditioning was performed with busulfan (cum. 6.4–8 mg/kg) in combination with fludarabine (cum. 150–180 mg/m<sup>2</sup>), or was performed according to Slavin et al. [15] or McSweeney et al. [16]. All protocols with cumulative busulfan dosages <12 mg/kg were defined to be dose reduced.

Thus, the majority of patients of the present study were males >40 years, in first chronic phase, and received PBSC from matched unrelated donors within the first year from diagnosis of CML.

According to the first German consensus meeting on immunogenetic donor search (1997), in the related setting, serological HLA-A, HLA-B, and low-resolution molecular genetic HLA-DRB1 typing was compulsory, and donor selection had to be based on the typing results for these HLA loci (two -A, two -B, two -DRB1). In the unrelated setting, HLA-A, -B, -DRB1, and -DQB1 was compulsory with HLA-A and -B being done with serological methods, and -DRB1 and -DQB at high resolution. Donors should be selected according to HLA-A, -B, and -DRB1 results (six HLA loci). If more than one HLA-A, -B, and -DRB1 identical donor was identified, donors also matched for -DQB1 should be preferred [17]. According to the second consensus (1999), matched donors were required to have the same HLA-A, -B, -DRB1, and -DQB1 antigens [18].

### Statistical analysis

As this study was an exploratory analysis, no sample size calculation was performed. Endpoints were overall survival (OS), event-free survival (EFS), transplant-related mortality (TRM), incidence of relapse, and incidence and severity of acute GvHD. Characteristics of patients were expressed as median and range for continuous variables and frequencies for categorical variables. Categorical data were compared by the  $\chi^2$  test or Fisher's exact test. Survival curves were estimated by the Kaplan–Meier method. The log-rank test was used to compare survival curves. The cumulative incidence method was used to estimate the incidence of TRM and relapse to account for competing event.

In a first step, the following factors were included in univariate analyses: patient's age, patient's sex, sex mismatch vs. match, donor type, time from diagnosis to SCT, disease status at SCT, stem cell source (bone marrow vs. PBSC), conditioning with vs. without TBI, standard vs. reduced intensity conditioning, and year of SCT. Additionally, patients' outcome was correlated with the Gratwohl (EBMT) score based on the variables donor type, disease stage, age, sex status, and time from diagnosis to SCT (only patients with related SCT or matched unrelated SCT were included in this correlation) [19].

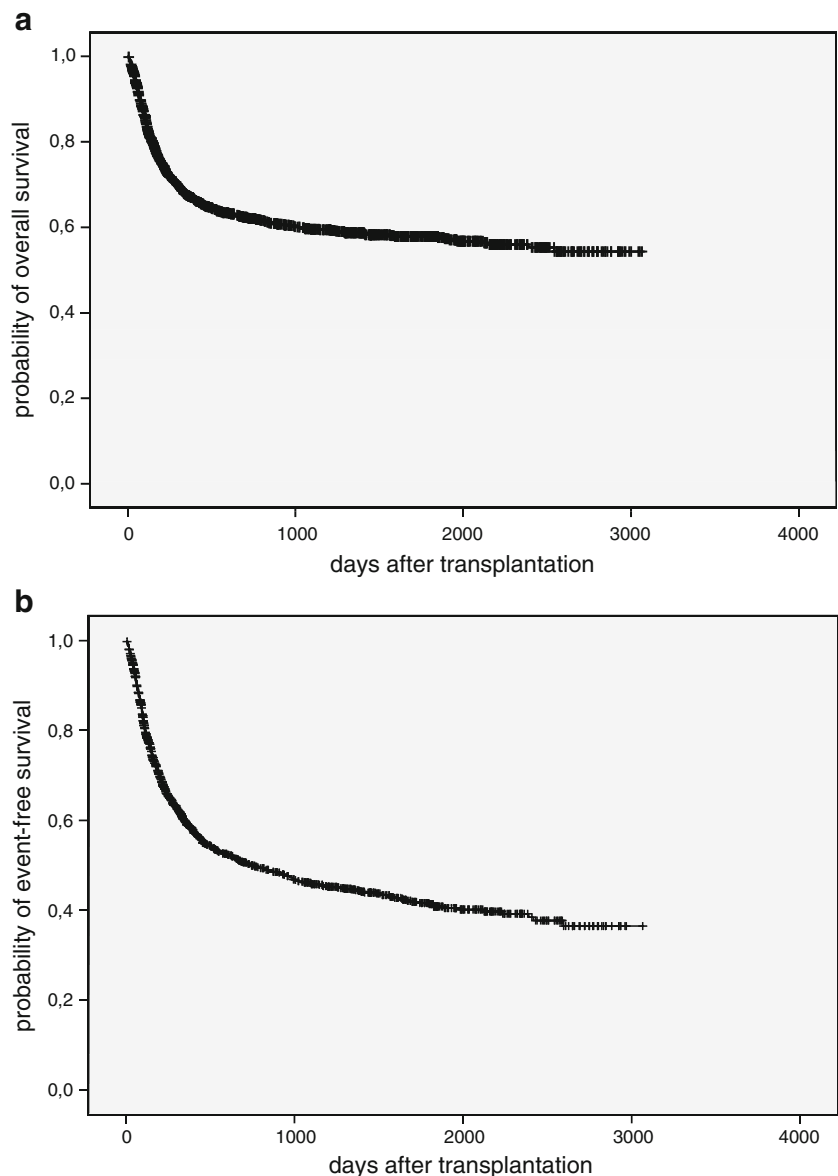
In a second step, all variables with a  $p$  value  $\leq 0.05$  were entered in a multivariable Cox regression model (forward elimination) to determine independent predictors. From this

analysis, variables for conditioning were excluded, as the amount of patients with known data was noticeably low. For reason of shortness, only the results of the final models are presented as relative risks (hazard ratios) with respect to a reference category ( $HR = 1$ ) together with the 95% confidence interval (CI) and  $p$  values.

Calculations were performed with SPSS, version 12 (SPSS Inc., 444 North Michigan Avenue, Chicago, IL 60611, USA). The competing risk analyses were done with ACCorD (V. Gebski, NHMRC Clinical Trials Centre, University of Sydney).

In spite of multiple testing, no adjustment of type I error was done. Therefore, results should be treated with caution.

**Fig. 1** Probability of **a** overall survival (OS) and **b** event-free survival (EFS) for patients with CML, transplanted in the period 1998–2004



## Results

### Development between 1998 and 2004

Between 1998 and 2004, the annual SCT rate was decreasing from 357 to 98, which corresponded to 28% of initial transplantations. This reduction was predominantly due to the decrease of annual transplantations in first chronic phase from 223 in 1998 to 45 SCTs in 2004 (20%). In contrast, the reduction of SCTs in advanced stages (>1. CP, AP, BP) was less significant with a decrease from 112

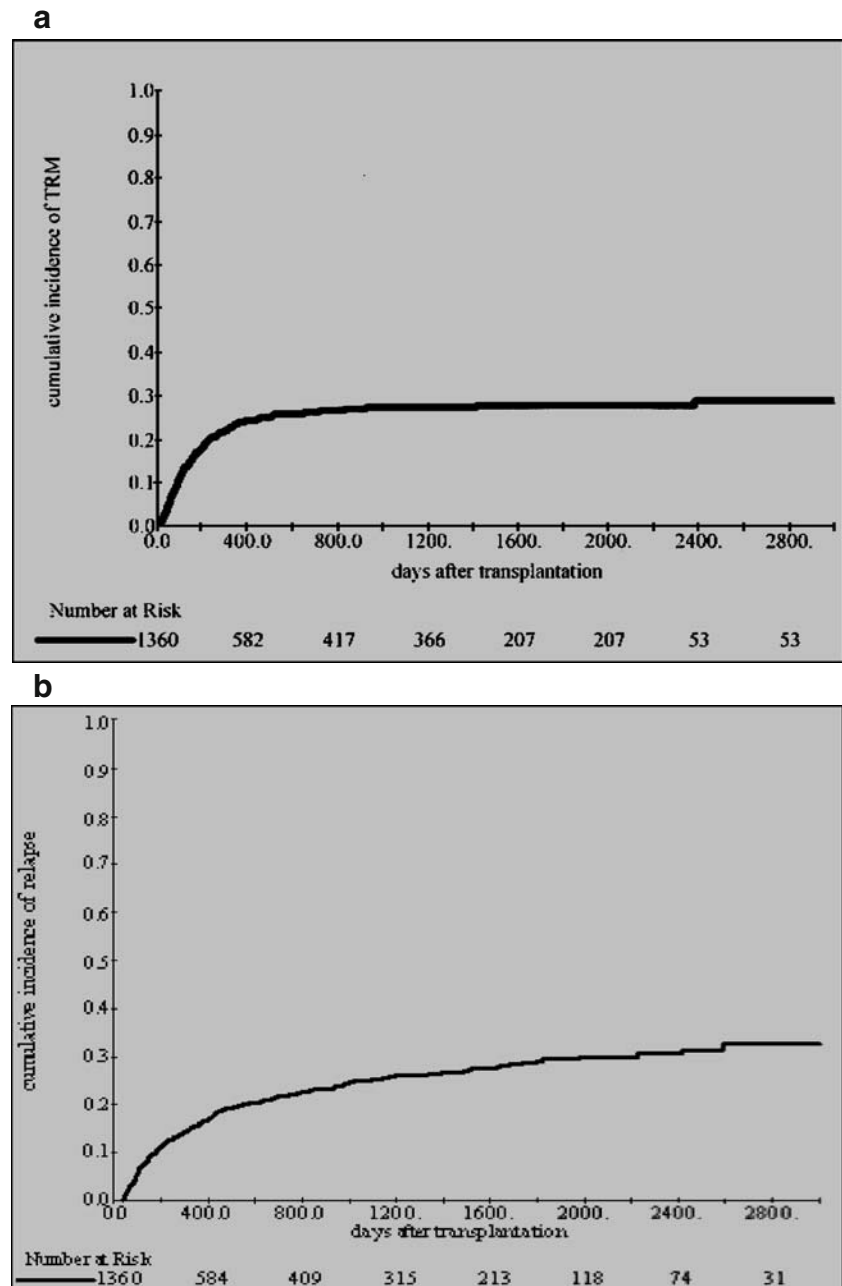
(1998) to 50 SCTs (2004) and consequently to 45% of the initial transplantation rate only.

Thus, the proportion of SCTs in advanced stages was increasing from 112/346 (32%) to 50/94 (53%) in the 6-year period of study.

### Outcome and complications

Data of leukocyte engraftment ( $>1 \times 10^9/l$ ) were available in 1,426 cases. Median leukocyte engraftment was reported on day + 15 after SCT (range 8–69 days). Acute graft-versus-

**Fig. 2** Cumulative incidence of **a** TRM and **b** relapse for patients with CML, transplanted in the period 1998–2004



host disease (GvHD) grade II–IV was seen in 555/1,428 (39%) of stem cell recipients (grade II = 20%, grade III = 11%, grade IV = 8%).

After a follow-up period of 5 years, 605 of 1,671 patients with available results had died, so 5-year OS was 58% (95% CI = 55–61%) (Fig. 1a). As 705/1,379 were alive without relapse, the 5-year EFS was 41% (95% CI = 38–44%) (Fig. 1b).

Of a total of 1,360 patients, 339 died from transplantation-related causes. The cumulative TRM incidence for 100 days, 1 year, and 5 years after SCT was 11% (95% CI = 9–13%), 24% (95% CI = 22–26%), and 28% (95% CI = 25–31%), respectively (Fig. 2a).

Relapse was documented in 340/1,380 of patients (25%). The 5-year cumulative incidence of relapse was 29% (95% CI = 26–32%) (Fig. 2b). The median follow-up of living patients was 27 months, with a range from 2 weeks to 102 months.

### Parameters influencing prognosis

For the definition of parameters influencing OS, univariate and multivariate analyses were performed.

According to univariate analysis, female sex, female donor/male recipient, patients' age <40 years, 1. CP at transplantation, and the performance of transplantation with bone marrow as stem cell source from an HLA-matched related donor within the first year after diagnosis in standard conditioned patients were significantly associated with higher 5-year OS rates in statistical analyses ( $p \leq 0.05$ ). Higher risk groups according to the Gratwohl

(EBMT) score (0–1, 2, 3, 4, and 5–7) were significantly correlated with worse OS ( $p < 0.001$ ) (Table 2).

In multivariate analysis, OS was improved for the following parameters: younger age, SCT in 1. CP, HLA-matched SCT, and SCT in the first year from diagnosis ( $p \leq 0.001$ ). Patients' sex, stem cell source (BM/PBSC), and donor types (related/unrelated) did not improve the model fit (Table 3).

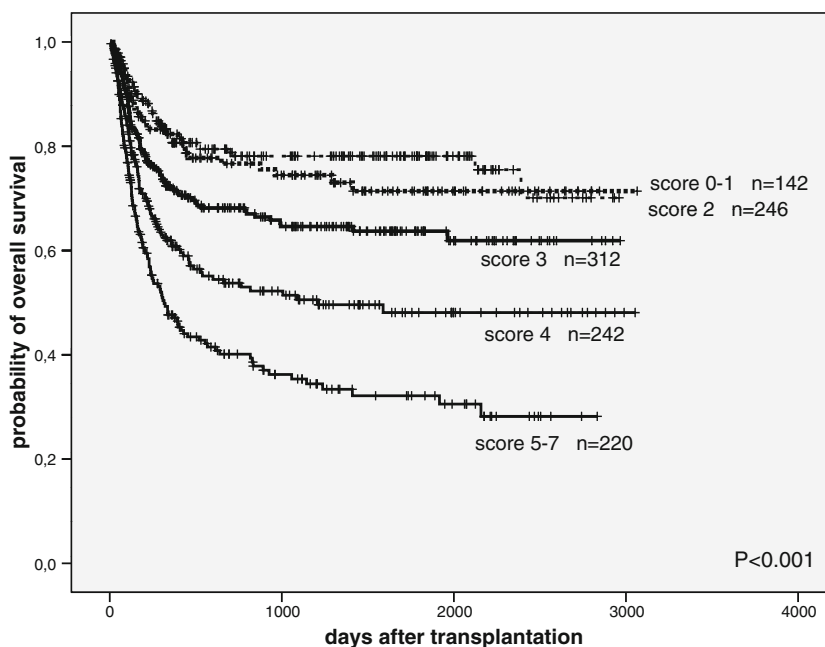
Comparison of patients with standard and reduced intensity conditioning

Comparison of the conditioning regimens showed improved 5-year OS for patients who received standard conditioning (62%; 95% CI = 58–66%) when compared to the cohort receiving reduced conditioning (RIC) (42%; 95% CI = 33–51%) ( $p < 0.001$ ).

This result had to be seen in association to significant differences in the risk profiles of standard and reduced conditioned patients (Table 4): patients with RIC were more frequently in advanced disease (>1. CP), had a longer history of disease, and received SCT more frequently >1 year from diagnosis. Also, a significant higher proportion of RIC patients was >40 years of age ( $p \leq 0.001$ ). Median leukocyte engraftment was independent from the type of conditioning (day +15 in both groups). Severe GvHD (grade II–IV) (36% vs. 37%) did not differ significantly between reduced and standard conditioned patients.

In contrast, HLA matching, stem cell source (BM/PBSC), donor types (related/unrelated), or TBI within the conditioning regimen showed no significant differences between the RIC and SIC cohorts.

**Fig. 3** Probability of overall survival (OS) for patients with CML according to the Gratwohl (EBMT) risk score





**Table 3** Overall survival (OS) of patients with CML, multivariate analysis

Parameter	Number of patients	Relative risk	95% CI	<i>p</i>
Age				
Continuous	1,443	1.010	1.002–1.017	0.011
Remissions status				
CP1	945	1		<0.001
Others	498	2.361	1.984–2.809	
Interval from diagnosis				
≤1 year	709	1		<0.001
>1 year	734	1.386	1.161–1.655	
HLA matching				
HLA match	1,216	1		<0.001
HLA mismatch	227	1.511	1.223–1.867	

CP1 1 chronic phase; SCT allogeneic stem cell transplantation; CI confidence interval

## Discussion

Due to the introduction of tyrosine kinase inhibitors, allo-SCT has been shifted to a second-line strategy for high-risk patients and those who failed therapy with IM. This change of treatment strategy provides the background for this retrospective overview on current transplantation activities and strategies within the German Registry of Stem Cell Transplantation (DRST) in 1,716 adult and pediatric patients being registered between 1998 and 2004.

First, within this period, annual transplantations showed a decrease from 357 to 98, which meant a reduction to

28%. This was comparable to an EBMT study which documented a decrease from ~1,400 to ~800 annual SCTs for CML in chronic phase in the period 1999–2003 [3], and a CIBMTR study showed a reduction from 617 annual SCTs in 1998 to 223 in 2003 [4, 20]. Likewise, to the results of previous analyses, the reduction of annual SCTs was most significant in first chronic phase to 20% of the initial transplantation rate, whereas the decrease in advanced phases was less significant (45% of the initial transplantation rate). Thus, the proportion of advanced phases showed an increase from 32% to 53% in this period. The CIBMTR documented as well an increase of SCTs for

**Table 4** Comparison of frequencies between patients with standard (SIC; maximal number 747) and reduced intensity conditioning (RIC; maximal number 156)

		SIC		RIC		<i>p</i>
		Number	%	Number	%	
Disease status	1. CP	509/733	69%	69/151	46%	<0.001
	Others	224/733	31%	82/151	54%	
	Unknown	14	–	5	–	
HLA matching	Match	629/746	84%	139/156	89%	0.14
	Mismatch	117/746	16%	17/156	11%	
	Unknown	1	–	–	–	
Stem cell source	BM	269/745	36%	50/155	32%	0.41
	PBSC	476/745	64%	105/155	68%	
	Unknown	2	–	1	–	
Donor type	Unrelated	412/746	55%	89/156	57%	0.72
	Related	334/746	45%	67/156	43%	
	Unknown	1	–	–	–	
Patient's age	1–19 years	58/747	8%	3/156	2%	<0.001
	20–39 years	320/747	43%	29/156	19%	
	40–59 years	359/747	48%	94/156	60%	
	>59 years	10/747	1%	30/156	19%	
TBI in conditioning	Without TBI	452/745	61%	85/156	55%	0.25
	With TBI	293/745	39%	71/156	46%	
	Unknown	2	–	–	–	
Interval from diagnosis	≤1 year	407/747	55%	49/156	31%	<0.001
	>1 year	340/747	45%	107/156	69%	

patients in 2. CP and AP from 24% to 41% [4], and the above EBMT study showed a greater decrease for allo-SCT in first chronic phase than in advanced disease [3]. These results suggest that allo-SCT still remains an important salvage option for patients in advanced CML.

Another focus were current strategies concerning donor types and stem cell sources. PBSC were already more frequently used than BM (38% vs. 62% of all SCTs), while the stem cell source (BM/PBSC) had no significant influence on survival in multivariate analyses. These data correspond to a retrospective study of Remberger et al., where PBSC and bone marrow from unrelated donors were associated with similar rates of GvHD, relapse, and survival [21]. In contrast, Elmaagacli et al. found improved overall survival with PBSC as stem cell source (94% vs. 66%) due to a significantly improved immune reconstitution for PBSC and a lower TRM consequently to infections and severe aGvHD [22]. Others suggested that the influence of stem cell source might depend on the phase of disease and the interval between diagnosis and SCT.

A CIBMTR study had shown that while in patients with CML in 1. CP the risk of treatment failure was similar with PBSC or BM with adjusted 1-year probabilities of DFS of 63% and 74%, respectively, there was an advantage for patients in advanced phases with adjusted 1-year probabilities of DFS of 68% with PBSC and 23% with BM. Causes of death after blood stem cell and bone marrow transplantation were similar [23]. These controversial results might reflect different conditioning strategies and selection criteria within the diverse studies. Thus, efforts to determine whether subsets of CML patients might benefit from either stem cell source should continue.

Further, in this analysis, SCT in CML was more frequently performed from unrelated than from related donors (55% vs. 45%), without any influence on survival in accordance to previous reports [13, 14, 24]. However, others suggested worsening of prognosis by unrelated SCT in subgroups of patients: An NMDP study described for those CML patients in chronic phase undergoing early transplantation in the first year from diagnosis a similar or only slightly inferior 5-year DFS after matched unrelated vs. matched sibling transplantation, while there was a substantially worse 5-year DFS after matched URD in case of delayed SCT. Thus, 5-year DFS was 39% for unrelated vs. 63% for related SCT in CP of CML when the delay was 1–2 years due to a significantly increased risk of graft failure and acute GvHD [25]. Mechanisms as immune compromise due to replacement of normal dendritic cells or natural killer cells with *BCR-ABL*-positive effectors were suggested as possible explanations. Therefore, it should be further evaluated whether distinct subgroups of CML patients still might have a benefit from related SCT.

We then focused on the actual position of reduced conditioning in CML. Reduced conditioning strategies were documented in 17% of SCTs in this study, so it was obvious that RIC has found entrance in the transplantation schedules in CML. The proportion of RIC was rather constant between 11% and 23% of all transplantations within the 6-year period of the study. In contrast, EBMT data had shown an increase of reduced conditioning strategies from 1% to 31% from 1998 to 2003 [20], which probably can be explained by the later introduction of reduced conditioning in some European countries when compared to the centers contributing to the DRST.

There first seemed to be a survival advantage for the standard conditioned patients when compared to reduced conditioning (5-year OS of 62% vs. 42%;  $p < 0.001$ ). However, the risk profiles of the RIC patients were less favorable according to age, phase of disease, and intervals from diagnosis of CML to SCT, which has to be considered. Relapse rates did not differ significantly between RIC and SIC patients (17% vs. 27%) in this study when all CML stages were considered. This might be diverse when advanced disease is taken into account: a Czech study including 295 patients with advanced CML found a 45% relapse rate in reduced conditioned patients when compared to standard conditioning, where no relapse occurred [26]. Also, the frequency of severe aGvHD (grade II–IV) was equal in reduced and standard conditioned patients (37% vs. 36%) in this DRST analysis. However, previous reports of similar frequencies of severe GvHD (grade II–IV) of 14%–19% irrespective of the intensity of conditioning [27] are in contrast to other studies where severe GvHD (grade II–IV) was significantly less frequent after reduced conditioning [28].

Thus, at this time, the optimal transplantation strategy for advanced CML cannot be precisely defined, but dose-reduced strategies should be further explored for these complex cases. Also, the application of tyrosine kinase inhibitors (TKIs) of the first [29–32] or second generation [33] as preemptive strategy in the post-transplant period deserves further attention.

In conclusion, this overview gives further confirmation that, despite being removed from first-line strategies since the introduction of imatinib, allo-SCT still plays an important role in higher advanced CML [34]. In addition, survival seems to be significantly influenced by the phase of disease at diagnosis, intervals between diagnosis and SCT, patients' age, and the Gratwohl (EBMT) risk score, while peripheral blood stem cells and unrelated transplantation are already predominant in CML with an equal outcome when compared to bone marrow as stem cell source or related transplantation. Finally, reduced conditioning has found its place in allo-SCT in CML and will probably be further developed in the future, which might

contribute to the needs of the high-risk patients now being in the focus of allo-SCT in CML.

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