Prognosis of acute myeloid leukemia patients up to 60 years of age exhibiting trisomy 8 within a non-complex karyotype: individual patient data-based meta-analysis of the German Acute Myeloid Leukemia Intergroup

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ABSTRACT

Background and Objectives

Trisomy 8 (+8) is among the commonest genetic aberrations seen in acute myeloid leukemia (AML). However, the prognostic significance of this aberration and the best consolidation strategy for patients with it are still not resolved. Additional prognostic indicators are needed to further classify these patients and determine their appropriate management.

Design and Methods

Individual patient data-based meta-analysis was performed on 131 patients (median age 50 (18-60) years) with +8 as a sole aberration or +8 with one additional aberration treated between 1993 and 2002 in eight prospective German AML treatment trials. All patients received state-of-the-art treatment including high-dose cytarabine with the option for autologous or allogeneic hematopoietic stem cell transplantation (HSCT).

Results

In total, the 131 patients had a 3-year overall survival (OS) of 29% and a 3-year relapse-free survival (RFS) of 32%. Independent prognostic factors contributing to shorter OS were age ≥45 years, extramedullary disease, and a percentage of +8 positive metaphases ≥80%. Combining these three prognostic variables established a hierarchical model for OS. The 3-year OS was 13% for the high-risk group, 36% for the intermediate-risk group, and 55% for the low-risk group (p<0.0001). Age <45 years and allogeneic HSCT (as treated) were independent prognostic factors for longer RFS. Additional cytogenetic aberrations other than t(8;21), inv(16), t(16;16), t(15;17) or 11q23 had no influence on treatment outcome.

Interpretation and Conclusions

We provide a new prognostic model for risk stratification of AML patients with +8. The data indicate that allogeneic HSCT may prolong RFS compared to that achieved with other strategies of post-remission therapy.

Key words: acute myeloid leukemia, trisomy 8, treatment outcome, prognostic factors, post-remission therapy.

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Trisomy 8 (+8) is one of the most frequent recurring aberrations in acute myeloid leukemia (AML).[1-4] Although additional aberrations are often found together with +8, many patients have +8 as a sole aberration. There is some evidence that patients with trisomy 8 occurring together with other cytogenetic aberrations have the prognosis confermed by the accompanying aberration. This is certainly true for the favorable cytogenetic aberrations t(8;21), inv(16) or t(15;17). The favorable prognosis of patients with these aberrations is basically not changed by an additional +8.[5;6] Additional 11q23 aberrations, such as t(9;11), also seem to confer a more favorable prognosis.[1] However, the occurrence of +8 within complex karyotypes with three or more independent aberrations does not improve the desperate prognosis of patients with such a complex karyotype.[1] There are reports showing an unfavorable prognosis for patients with +8 together with high risk aberrations, such as -7, -5 or del(5q),[7] although due to low numbers of patients this observation cannot yet be regarded as proven. For AML with +8 as a sole aberration it is still unclear whether +8 is the primary event leading to AML or not. However, until now no cryptic rearrangements or mutations have been found to support the second hit hypothesis of trisomy 8.[8] In contrast, gene expression experiments do support the idea that overexpression of genes on chromosome 8 is involved in the development of AML.[9;10] Thus, +8 as a sole aberration should still be regarded as a cytogenetic entity. It is associated with low white blood cell counts, a low percentage of bone marrow blasts and a high frequency of multi-drug resistance gene (*MDR1*) expression.[4;11]

The prognosis of AML patients with +8 as a sole aberration or with +8 and one additional aberration other than t(8;21), inv(16), t(16;16), t(15;17) or 11q23 aberrations is still a matter of debate. Some groups, such as the MRC and SWOG, have assigned these patients to a group with an intermediate prognosis,[2,4] whereas the GALGB group consider that they have an unfavorable[1,12] treatment outcome. So far only one literature search has evaluated independent prognostic factors among AML patients with +8 as a sole aberration revealing trisomy 8 clonal size as a potential predictor in a small number of cases.[13]

This unclear prognostic situation is accompanied by an unclear therapeutic situation. Conventional consolidation with high-dose cytarabine seems not to cure the disease, and only anecdotal data are available regarding transplantation strategies in small numbers of patients within each single trial.[14]

Therefore, we performed a meta-analysis of individual AML patients with trisomy 8 as a sole aberration or with +8 and one additional aberration treated within the German AML trials. The aim was to reveal new prognostic factors for survival including clinical, cytogenetic and laboratory data and also to compare different consolidation strategies, i.e. high-dose cytarabine and autologous or allogeneic hematopoietic stem cell transplantation (HSCT).

Design and Methods

Selection of patients and review of data

Between April 1993 and December 2002, AML patients were prospectively enrolled in one of the eight following German multi-center trials: AMLHD93[15] and AMLHD98A[16] of the Acute Myeloid Leukemia Study Group (AMLSG) Ulm, AML 2/95[17] and AML 1/99 of the Southern German Hematoblastosis Group (SHG) Hannover, AMLCG92[18] and AMLCG2000[19] of the Acute Myeloid Leukemia Cooperative Group (AMLCG), AML96[20] of the German Study Initiative Leukemia (DSIL) Dresden and AML-(033)-96 of the Eastern German Study Group for Hematology and Oncology (OSHO). The more recent trials AMLHD98A (NCT 00146120), AML 1/99 (NCT 00209833), AMLCG2000 (NCT 00266136), AML96 (NCT 00180115) and AML-(033)-96 (German Study Registry) were all registered in a public trials registry in accordance with the guidelines of the ICMJE. The trials AMLHD93, AML 2/95 and AMLCG92 were closed in 1999 or earlier, and their results have been already published. All trials were performed after approval by a local Human Investigations Committee and are in accordance with the Helsinki Protocol.

The inclusion criteria of the different trials were concordant, and the inclusion criteria for this survey were as follows: (i) presence of trisomy 8 on standard karyotypic analysis; (ii) absence of t(8;21), inv(16), t(16;16), t(15;17) or 11q23 abnormalities representing defined AML subclasses according to the WHO classification;[21] (iii) absence of a complex karyotype with at least three independent cytogenetic aberrations; (iv) age 16 to 60 years; (v) availability of clinical data. Demographic, diagnostic, clinical and laboratory data, cytogenetics, type of induction and post-remission therapy and information about treatment outcome were collected for each patient, sent to a central co-ordinating center and reviewed for consistency and completeness before analysis.

Treatment protocols

All patients received double induction therapy and high-dose cytarabine during the treatment course. All protocols provide the option for autologous and/or allogeneic stem cell transplantation within consolidation therapy. The protocols are summarized in Figure 1, and numbers of patients per protocol are given in Table 1.

Cytogenetics

In four of the five study groups cytogenetic studies were performed in central reference laboratories (AMLSG Ulm, AMLCG, SHG Hannover and DSIL Dresden). In one group (OSHO) cytogenetic analyses were done on an institutional level. The description of the karyotype followed the recommendations of the

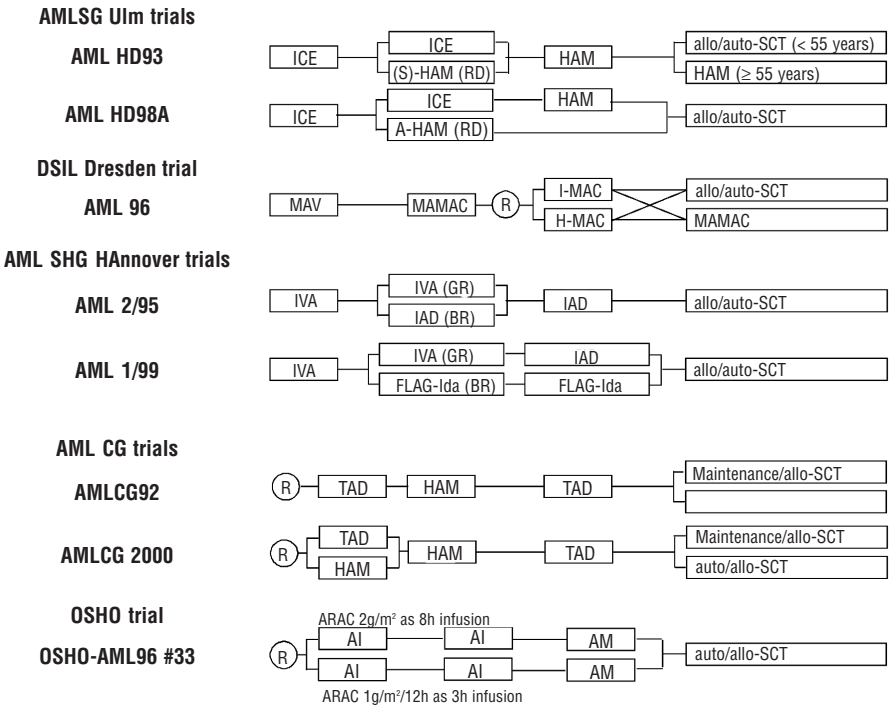

Figure 1. Summary of the eight prospective treatment trials of the German AML Intergroup. ICE: idarubicin, cytarabine, etoposide; HAM: high-dose cytarabine and mitoxantrone; S-HAM: sequential HAM; (S)-HAM: sequential HAM for patients <55 years and HAM for patients ≥55 years, respectively; A-HAM: ATRA, high-dose cytarabine and mitoxantrone; MAV: mitoxantrone, cytarabine, etoposide; MAMAC: m-AMSA and high-dose cytarabine; I/H-MAC, 12 g/m²/36 g/m² high-dose cytarabine and mitoxantrone; IVA: idarubicin, etoposide, cytarabine; IAD: intermediate-dose cytarabine, daunorubicin; FLAG-Ida: fludarabine, intermediate-dose cytarabine, idarubicin; TAD: thioguanine, cytarabine, daunorubicin; AI: cytarabine and idarubicin; AM: cytarabine and mitoxantrone; GR: good responder; BR: bad responder; RD: resistant disease; auto-SCT: autologous stem cell transplantation; allo-SCT: allogeneic stem cell transplantation.

International System for Human Cytogenetic Nomenclature.[22]

Analysis of *FLT3* mutations

FLT3-ITD and *TKD* mutations were analyzed centrally in Munich for the trials AMLCG92 and AMLCG99, in Hannover for the trial AML 1/99, in Ulm for the trials AMLHD93 and AMLHD98A, and in Dresden for the AML96 trial according to the previously published protocols.[23-25]

Statistical analyses

The definition of complete remission (CR) followed the recommended consensus criteria[26] and was evaluated after two induction cycles. Overall survival (OS) endpoints, measured from the date of entry into one of the prospective studies, were death (failure) and alive at last follow-up (censored).[26] Relapse-free survival (RFS) endpoints, measured from the date of documented CR, were relapse (failure), death in CR (failure) and alive in CR at last follow-up (censored).[26] Consolidation therapy was classified into high-dose cytarabine-based chemotherapy, autologous HSCT and allogeneic HSCT. For comparison analyses between these three consolidation strategies only patients in first CR with at least one course of consolidation therapy were considered. In all trials patients received high-dose cytarabine as chemotherapy consolidation. In some trials patients who had a moderate or no response to the first induction cycle received intermediate- or high-dose cytarabine as the second induction cycle whereas patients with a good response received a second cycle of standard-dose cytarabine (Figure 1). Therefore, the influence of cumulative doses of cytarabine on the treatment outcome could not be evaluated. Logistic regression analyses were used to identify prognostic variables for CR rates. The Kaplan-Meier method was used to estimate the distribution of RFS and OS. Confidence interval (CI) estimation for the survival curves was based on the cumulative hazard function using Greenwood's formula for the SE estimation. Survival distributions were compared using the log rank test stratified for the variable study. Cox models were used to identify independent prognostic variables for survival. To provide quantitative information on the relevance of results, 95% CI of odds ratios and hazard ratios (HR) were computed. The prognostic model for OS was achieved by hierarchical cluster analysis. All statistical analyses were performed with the software package of SPSS Version 12.0.1.

Results

Patients' characteristics

Between April 1993 and December 2002, 145 adult AML patients aged 18 to 60 years with isolated +8 or +8 with one additional aberration other than t(8;21), inv(16), t(16;16), t(15;17) or 11q23 abnormalities were registered in the eight trials of the German AML Intergroup. Adequate clinical data were not available for 14 patients, leaving 131 eligible patients for this survey. Table 1 depicts their clinical data and characteristics. One hundred and twelve (85%) patients had *de novo* AML and 19 (15%) had secondary AML (15 with preceding MDS; 4 therapy-related). Data on extramedullary disease were available for 125 patients. An

Table 1. Patients' characteristics. Summary of the eight prospective treatment trials of the German AML.

	$\sum n$	*n*	%	*Median (Range)*
Treatment trial	131			
SHG-Hannover (AML 2/95 / AML 1/99)		13/13	10/10	
SHG-Dresden (AML96)		20	15	
AMLCG (AMLCG92 / AMLCG99)		16/29	12/22	
OSHO (AML96 #033)		15	12	
AMLSG Ulm (AMLHD93 / AMLHD98A)		4/21	3/16	
Sex (Male/Female)	131	69/62	53/47	
Age [years]	131			50 (18-60)
ECOG status	118			
0		28	24	
1		63	53	
2		20	17	
3		6	5	
4		1	1	
Disease status (secondary/*de novo*)	131	19/112	15/85	
FAB classification	127			
M0		2	2	
M1		26	20	
M2		37	29	
M4		22	17	
M5		30	24	
M6		5	4	
M7		5	4	
Extramedullary manifestation (yes/no)	125	19/106	15/85	
WBC count [10^9/L]	130			12.0 (0.1-427.0)
Platelet count [10^9/L]	129			46 (4-902)
Hemoglobin level [g/dL]	128			8.8 (3.8-15.5)
Bone marrow blasts [%]	114			80 (20-100)
Lactate dehydrogenase [U/L]	98			507 (115-8344)
FLT3-ITD and/or -*TKD* mutation (yes/no)	76	14/62	18/82	
Cytogenetics	131			
+8 as a sole aberration		92	70	
+8 with one additional aberration		39	30	
-7			1	
-5/del(5q)		3		
+8			3	
+21		3		
+22		3		
Other trisomies		7		
Other aberrations		19		

extramedullary manifestation of the AML was found in 19 (15%) patients. Sites of extramedullary manifestation were skin, mucosa, central nervous system and other organs. Data on *FLT3* mutational status were available for 76 patients. Fourteen (18%) patients were *FLT3* positive. Patients with *FLT3* mutation had a higher white blood cell (WBC) count than patients without *FLT3* mutation [78.0(0.8-427.0) 10^9/L vs. 10.1(0.9-198.0) 10^9/L; $p<.001$].

Cytogenetics

All 131 patients were diagnosed with conventional cytogenetics. Ninety-two (70%) had +8 as a sole aberration. One additional aberration was recognized in 39 (30%) patients. Of those patients, four had an additional high-risk aberration, such as –7, -5 or del(5q). No additional inv(3q) or t(3;3) was seen. Thirteen (33%) had other additional trisomies. Recurring additional trisomies were +21 in three patients and +22 in three patients (see Table 1). The largest group of 19 (49%) patients had other not recurring aberrations. In detail these were i(5)(p10), i(7)(q10), i(17)(p12), i(17)(q10), del(3)(q21), del(9)(q22q34), del(12)(p12), del(13)(q12q22), del(14)(q22), del(20)(q11), t(2;3)(q21;q13), t(5;6)(p10;p10), t(9;22)(q34;q11), t(11;?), t(17;19)(q23;q13), inv(9)(p11q13), -Y, -19 and +mar. Of all patients 58% had at least 80% +8 positive metaphases, whereas 42% presented with less than 80% affected cells within the blast cell population. There was no obvious clustering of the above-described high-risk aberrations within the group of patients with 80% and more +8 positive metaphases. The one patient with –7 had 100% +8 positive metaphases, whereas the percentages in the three patients with 5q- were 100%, 50% and 30%.

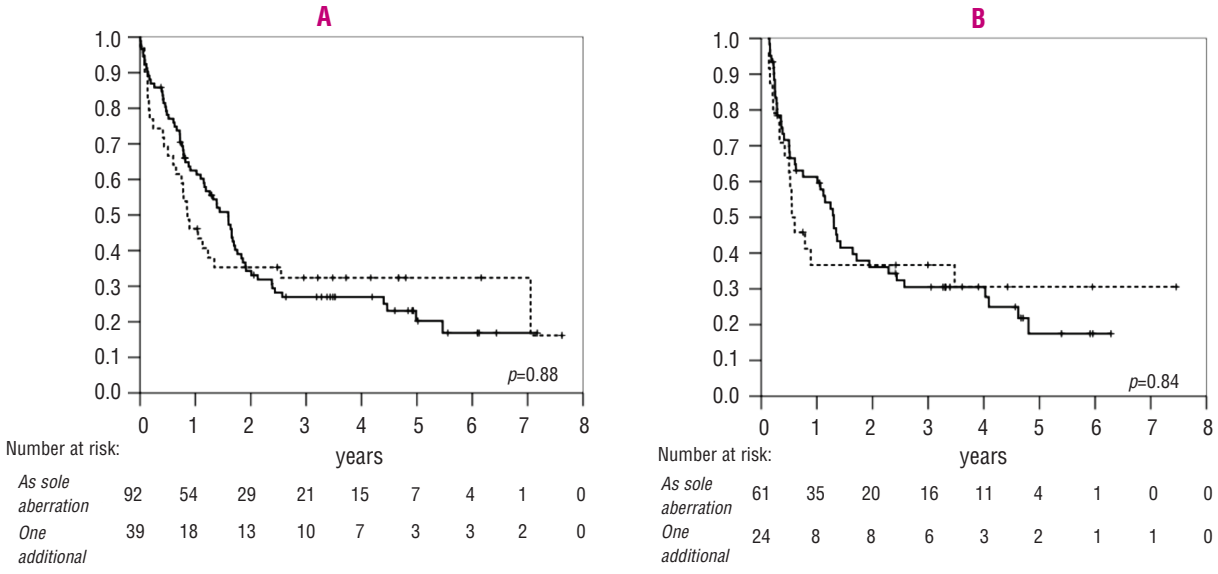

Figure 2. Overall (A) and relapse-free (B) survival of AML patients with trisomy 8 in relation to additional cytogenetic aberrations. Patients with +8 as a sole aberration (*solid line*), patients with +8 and one additional cytogenetic aberration other than t(8;21), inv (16), t(16;16), t(15;17) or 11q23 abnormalities (*dotted line*).

Induction therapy

After induction therapy 65% (85/131) of patients reached CR, 14% (18/131) experienced early or hypoplastic death and 21% (28/131) had resistant disease.

The following variables at diagnosis were evaluated for their potential influence on response to induction therapy: age, disease status, WBC count, platelet count, hemoglobin level, lactate dehydrogenase level, bone marrow blast count, percentage of +8 positive metaphases, extramedullary disease, *FLT3* mutation, additional cytogenetic aberrations and study. No variable had an independent prognostic impact on the treatment response.

Survival analysis

The median follow-up time for survival was 3.6 years. The 3-year OS and RFS rates were 29% (95%-CI 21-37%) and 32% (95%-CI 22-42%) for all 131 and the 85 patients in CR, respectively.

There was no significant difference in survival between patients with +8 as a sole aberration (n=92) and those with +8 and one additional cytogenetic aberration (n=39) [3-year OS: 27% (95%-CI 18-36%) vs. 32% (95%-CI 17-47%) p=0.88, and 3-year RFS 31% (95% CI 18-43%) vs. 37% (95% CI 17-56%) p=0.84, respectively] (Figure 2).

Out of 85 patients with CR, 72 were eligible for post-remission therapy. These patients had received at least one complete course of post-remission therapy. Forty-three (60%) received high-dose cytarabine, 10 (14%) autologous HSCT and 19 (26%) allogeneic HSCT (14 related and 5 unrelated). Allogeneic HSCT was performed at a median of 5.0 (2.5-8.0) months after diagnosis. Patients who underwent allogeneic HSCT were younger than patients who did not [32 (18-55) years vs. 51 (19-59) years p=0.001]. OS was not significantly different between the three post-remission strategies. The 3-year OS rates were 37% (95%-CI 23-52%) for high-dose cytarabine, 34% (95%-CI 3-65%) for autologous HSCT and 45% (95%-CI 22-68%) for allogeneic HSCT (p=0.63). Whereas the rate of treatment-related mortality was higher among patients who underwent allogeneic HSCT than those who did not within the first 3 years (27% vs. 4%; p=0.01), the former had a much lower probability of relapse (27% vs. 69%; p=0.002). This lower probability of relapse transformed into a better 3-year RFS for patients who were treated with allogeneic HSCT than patients who received autologous HSCT or high-dose cytarabine in the as-treated analysis [49%(95% CI 25-72%) vs. 23%(95% CI 0-51%) vs. 28%(95% CI 14-41%), p<0.05, respectively]. In the landmark analysis at 8 months with all allogeneic transplantations performed the 3-year RFS was 57% (95% CI 32-83%) for patients treated with allogeneic HSCT (n=15), 25% (95% CI 0-55%) for those undergoing autologous HSCT (n=8) and 42% (95% CI 26-58%) for those given high-dose cytarabine (p=0.12).

Prognostic variables for survival

Prognostic factors for survival were analyzed in the whole group of patients (n=131) as well as in the subgroup of CR patients who received at least one complete course of post-remission therapy (n=72). The following variables at diagnosis were evaluated: age, disease status, WBC count, platelet count, hemoglobin

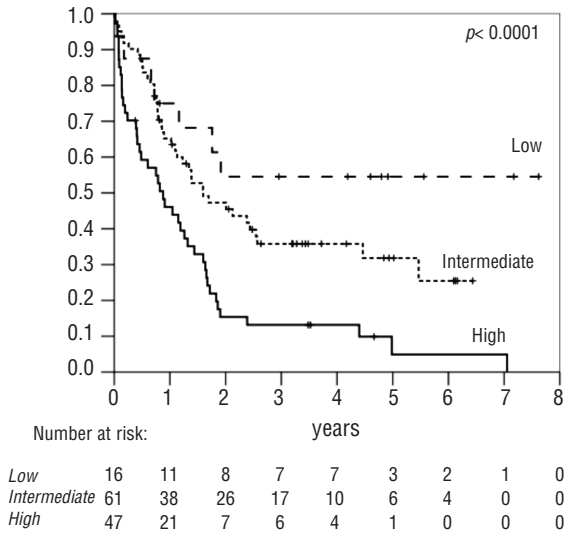

Figure 3. Prognostic model for overall survival of AML patients with +8. Low risk (*dashed line*): age < 45 years, no extramedullary disease and <80% +8 positive metaphases at diagnosis; high risk (*solid line*): age ≥45 years and extramedullary disease and/or ≥80% positive metaphases at diagnosis; Intermediate risk (*dotted line*): all other patients.

level, lactate dehydrogenase level, bone marrow blast count, percentage of +8 positive metaphases, extramedullary disease, *FLT3* mutation, additional cytogenetic aberrations and study. The variable post-remission therapy (high-dose cytarabine vs. autologous HSCT vs. allogeneic HSCT) was included in the second analysis. Continuous variables were included in the model continuously. Age and percentage of +8 positive metaphases were included dichotomized as cut-points were found in the hierarchical cluster analysis at 45 years (p=0.001) and 80% (p=0.04), respectively. The multivariate model for OS with limited backward selection revealed dichotomized age (≥45 years vs. <45 years) [HR 2.25 (95% CI 1.44-3.52) p<0.0001], extramedullary disease at diagnosis (yes vs. no) [HR 1.82 (95% CI 1.07-3.09) p=0.03] and dichotomized percentage of +8 positive metaphases (≥80% vs. <80%) [HR 1.60 (95% CI 1.05-2.45) p=0.03] as prognostic variables for the whole group of patients.

By combining these three independent prognostic factors a hierarchical model for OS with three risk-groups could be established. High risk patients with +8 were 45 years or older and had either extramedullary disease or ≥80% +8 positive metaphases at diagnosis (n=47), whereas low risk patients were younger than 45 years, had no extramedullary disease and <80% positive metaphases at diagnosis (n=16). All other patients, i.e. patients older than 45 years without extramedullary disease and <80% +8 positive metaphases or patients younger than 45 years with extramedullary disease and/or ≥80% +8 positive metaphases, were in an intermediate risk group (n=61) (p<0.0001) (Figure 3). Two patients (4%) in the high-risk group, four (25%) in the low-risk group and 12 (20%) in the intermediate-risk group received an allogeneic transplant in first CR. A significant influence of allogeneic HSCT on survival could not be recognized in any group (*data not shown*).

In the subgroup of patients in CR who had received at least one complete course of post-remission therapy only age (≥45 years vs. <45 years) [HR 2.14 (95% CI 1.17-3.93) p=0.01)] was a prognostic variable for OS. The strategy of post-remission therapy (high dose cytarabine vs. autologous HSCT vs. allogeneic HSCT) was not a prognostic factor. For RFS the model revealed age (≥45 years vs. <45 years) [HR 1.84 (95% CI 1.07-3.17) p=0.03] as a prognostic factor for the whole group of patients and allogeneic HSCT (as treated yes vs. no) [HR 0.45 (95% CI 0.22-0.93) p=0.03] as a prognostic factor for patients in CR who had at had least one complete course of post-remission therapy.

Discussion

The prognosis and optimum therapy of AML patients with +8 as a sole aberration or with +8 and one additional aberration other than t(8;21), inv(16), t(15;17) or 11q23 abnormalities are still difficult to define. The differences in prognosis of patients with +8 as a sole aberration or with + 8 and one additional aberration reported so far indicate that this population of patients is heterogeneous and might be further subdivided by additional prognostic factors.[1-4;7;12] The present survey reveals prognostic factors within a group of 131 AML patients with +8 as a sole aberration or with one additional aberration. Although this individual patient data-based meta-analysis is not a substitute for prospective trials, and some heterogeneity among the trials included has to be taken into account, it is the largest cohort of patients with +8 as a sole aberration or with one additional aberration presented so far.

The 65% CR rate of the patients included in this meta-analysis is in good accordance with other published results.[1,4,7] Like Byrd *et al.*[1] we found no influence of one additional cytogenetic aberration other than t(8;21), inv(16), t(16;16), t(15;17) or 11q23 abnormalities on treatment response.

The 3-year OS of 27% and RFS of 31% in patients with +8 as a sole aberration is also comparable to the reported data of the SWOG[4] and the CALGB.[1] Again there was no difference in survival between patients with +8 as a sole aberration and patients with +8 and one additional aberration.

Multivariate analysis including clinical, laboratory, cytogenetic and therapeutic variables identified age, extramedullary disease and the percentage of +8 positive metaphases at diagnosis as independent prognostic

factors for OS. By combining these three variables we have built a hierarchical prognostic model. Patients with +8 can be stratified into low, intermediate and high-risk groups. So far one published literature search on 56 cases of AML with +8 as a sole aberration has attempted a risk classification within this entity.[13] The author, like us, described a percentage of +8 positive metaphases ≥80% as a poor prognostic factor for survival. In this context it must be kept in mind that trisomy 8 was found to be constitutional in about 15-20% of patients with myelodysplasia or leukemia.[27] It is possible that such patients with an inherited mosaicism of +8 cluster within the low-risk group with less than 80% +8 positive metaphases. In these patients +8 might not be the prognosis-determinating aberration. Furthermore, a significant proportion of patients with +8 present with extramedullary disease and it is suggested that they might be predisposed to the development of leukemic skin infiltration.[28]

Thus the new risk factors and prognostic model presented here seem to be of clinical relevance and may allow risk-adapted treatment strategies for AML patients with trisomy 8 in the future. However, due to small numbers of allogeneic transplants within the risk groups, a possible confounding effect of allogeneic HSCT on the prognostic model cannot be ruled out. Compared to the incidence of AML with a normal karyotype, that of *FLT3* positive +8 is relatively low. In the analysis presented here we found that 18% of AML patients with +8 harbored *FLT3* mutations, which is in good accordance with published data.[25] *FLT3* mutations had no independent prognostic impact on survival among the patients examined. The strategy of post-remission therapy influenced RFS of patients with +8. Previously published data suggest that cytarabine-based chemotherapy is not able to cure AML with trisomy 8.[14] Virtaneva *et al.*[10] showed by expression profiling that an altered expression of apoptosis-regulating genes may be one possible cause for resistance to cytarabine in AML with trisomy 8.

In addition, we found a relation between the degree of trisomy 8 mosaicism and survival. Thus, the data of Virtaneva *et al*. and ours suggest that trisomy 8 may identify a sub-clone of chemotherapy resistant cells, the proportion of which may correlate with survival probabilities under cytarabine treatment.

It has been speculated that autologous or allogeneic HSCT in first CR might improve the prognosis of these patients. However, only three out of 42 patients with +8 as a sole aberration within the CALGB survey were transplanted.[14] A more recent survey of the same group showed a survival benefit from allogeneic HSCT compared to cytarabine-based chemotherapy in patients with common isolated trisomies, which included trisomy 8, 11, 13 and 21.[12] Within a homogeneous group of patients with +8 in first CR who had received at least one complete course of post-remission therapy, we found an independent positive impact of allogeneic HSCT compared to high-dose cytarabine or autologous HSCT on RFS, although not on OS in the as-treated analysis. This is probably due to the higher treatment-related mortality of the allogeneic compared to the autologous HSCT or high-dose cytarabine approach. As all patients in this survey received full dose conditioning before allogeneic transplantation, it can be speculated that with dose-reduced conditioning strategies a lower transplant-related mortality would produce better OS rates in the future. However, as it takes up to 8 months for patients receiving allogeneic HSCT, the influence of this treatment procedure on outcome may be subjected to a time-selection bias as suggested by the landmark analysis. Thus, although this is the largest cohort reported in the literature so far, we are aware that the numbers of patients are still small and that large, international, prospective studies on an intent-to-treat principle are eagerly desired to clarify the impact of allogeneic HSCT on treatment outcome in this group of patients.

In conclusion this individual patient data-based meta-analysis presents a large series of young adult AML patients with +8 as a sole aberration and with +8 and one additional cytogenetic aberration other than t(8;21), inv(16), t(16;16), t(15;17) or abnl11q23, receiving state-of-the-art therapy. In this survey, we found that AML patients with +8 do not form a homogeneous group and provide a new model for OS to stratify these patients into three prognostic groups. Furthermore, our data suggest that allogeneic HSCT may be the superior post-remission strategy for improving relapse-free survival.

Authors' Contributions

MS: conception and design, provision of study material and patients, collection and assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript; RFS: conception and design, provison of study material and patients, data analysis and interpretation, final approval of manuscript; KKA-A: provision of study material and patients, final approval of manuscript; HD: conception and design, final approval of manuscript; AG: conception and design, collection and assembly of data, final approval of manuscript; GH: provision of study material and patients, collection and assembly of data, final approval of manuscript; TI:collection and assembly of data, data analysis and interpretation, final approval of manuscript; RK: collection and assembly of data, final approval of manuscript; JK: conception and design, provison of study material and patients, collection and assembly of data, final approval of manuscript; CS: collection and assembly of data, data analysis and interpretation, final approval of manuscript; TB: conception and design, provison of study material and patients, data analysis and interpretation, final approval of manuscript; GE: conception and design, provison of study material and patients, collection and assembly of data, data analysis and interpretation, final approval of manuscript.

Conflict of Interest

The authors reported no potential conflicts of interest.

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