Characterization and prognostic implication of 17 chromosome abnormalites in myelodysplastic syndrome

Running title: Chromosome 17 abnormalities in MDS

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ABSTRACT

The prognosis of chromosome 17 (chr17) abnormalities in patients with primary myelodysplastic syndrome (MDS) remains unclear. The revised International Prognostic Scoring System (IPSS-R) includes these abnormalities within the intermediate cytogenetic risk group.

This study assessed the impact on overall survival (OS) and risk of acute myeloid leukemia transformation (AMLt) of chr17 abnormalities in 88 patients with primary MDS. We have compared this group with 1,346 patients with primary MDS and abnormal karyotype without chr17 involved.

Chr17 abnormalities should be considered in the high-risk cytogenetic category. Monosomy 17 should be included within very-poor prognosis and i(17q), as no-complex karyotype should be continued within the intermediate-risk group.

INTRODUCTION

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem cell disorders (ref. 1-3). The prognosis and clinical course of MDS is highly variable and several scoring systems have been developed to assess the prognosis (ref. 4-7). The International Prognostic Scoring System (IPSS) has become the gold standard for risk assessment in patients with *de novo* MDS (ref. 4). However, one of the main pitfalls of this scoring system is that it includes different chromosomal aberrations without knowing the prognostic implications. Abnormalities of chromosome 17 (chr17) occurs in 2% of patients with *de novo* MDS and belong to the intermediate cytogenetic risk group according to the IPSS. The prognosis of chr17 abnormalities in patients with primary MDS remains unclear with great discrepancies between published studies (ref. 8-21). A recent study about prognostic value of i(17q) in MDS gives it in the intermediate prognostic group (ref. 22). The aims of this work are to assess the characteristics of a series of 88 patients with *de novo* MDS and chr17 abnormalities, to analyze the prognostic value of different chromosome 17 aberrations, and to study their prognostic impact compared to 1,346 patients with primary MDS and an abnormal karyotype but without abnormalities of chr17.

MATERIAL AND METHODS

Data Collection

The Spanish Registry of MDS is a database of the Spanish cooperative group on MDS. This database includes retrospective and prospective clinical and biological data from patients diagnosed of MDS at the participating institutions.

Patients and diagnostic criteria

A study group of 88 patients with primary MDS and an abnormality of chr17 along with a control group of 1,346 patients with primary MDS and an abnormal karyotype but without abnormalities of chr17 included in the database of the Spanish Registry of MDS constitute the population of the present report. The diagnosis of MDS was made according to WHO 2001 criteria (ref. 2). The following work is a retrospective study. We did not a specific study of the anomalies of the chr17 for lack of sufficient morphological data. However, several studies showed that some alterations of the chr17 are associated with the presence of hypercellularity, pseudo–Pelger–Huët, cells containing small vacuoles, prominent basophilia and eosinophilia, and marked increase of micromegakaryocytes (ref. 13-16).

In all patients included in this study, cytogenetic abnormalities have been detected by conventional cytogenetic procedure. The criteria defined by the International System for Human Cytogenetic Nomenclature in 2009 were used for identification of abnormal clones (ref. 23-24).

In keeping with the guidelines of the Declaration of Helsinki, this retrospective non-interventional study was conducted with the approval of the internal review board from the participating institutions belonging to Spanish Registry of MDS.

Prognostic factors

The main prognostic factors evaluated for OS and AML transformation, recorded at the time of diagnosis, are summarized in Table 1. Classification systems included WHO 2001 (ref. 2) and IPSS scoring system (ref. 4).

Statistical analysis

Comparisons of proportions and ranges of variables between different groups were performed by Chi-square, Fisher, Student's t-test, Mann-Whitney U-test or One-Way ANOVA as appropriate.

The Kaplan-Meier product limit method was used to estimate the probability of OS and risk of AML transformation, OS was measured from hematological diagnosis to death or last follow-up. All deaths, whether related or not to MDS, were considered as the endpoint of the follow-up interval. AML transformation was measured from diagnosis to AML development. Patients dying from any cause before developing AML were considered as censored data in the date of death for the calculation of AML transformation curves. Statistical comparisons between different actuarial curves were based on log-rank tests.

Multivariate analysis using the Cox proportional hazards regression method for temporal events was used to identify the most significant independent prognostic variables for OS and AML transformation.

The selected p value for considering differences as statistically significant in all analyses was $p<0.05$. All analyses were performed using the statistical package PASW version 18.0 (IBM Corporation, Armonk, NY. USA).

RESULTS

Characteristics of the patients with abnormality of chr17

The main characteristics of the patients at the time of diagnosis are summarized in Table 1. The series included 57 males (64.8%) and 31 females (35.2%) with a median age of 71.8 years (range: 23–92 years). The median value for hemoglobin level, ANC and platelet count was 9.0 g/dL, 1.97 x 10^9 per liter and 112 x 10^9 per liter, respectively, whereas median BM blast count was 7.1%. Most of the patients were classified as RAEB (69.3%) or RA (23.9%) according to the FAB classification; and RAEB-1 (28.6%) or RAEB-2 (44.0%) by WHO criteria. The IPSS risk group was intermediate-1 in 19 patients (22.1%), intermediate-2 in 35 patients (40.7%) and high risk in 32 patients (37.2%).

In total, 72 patients (81.8%) had a loss of short arm of chr17 and 16 patients (18.2%) did not have this loss.

In relation to karyotype complexity, 18 patients (20.5%) had an abnormal chr17 as isolated chromosomal abnormality, 8 (9.1%) had one additional abnormality and 62 (70.4%) had a complex karyotype with two or more associated abnormalities. The most frequent additional abnormalities to chr17 were deletion 5q (n=38), deletion 7 or -7 (n=24), trisomy 8 (n=18), deletion 18q or -18 (n=14), abnormalities chr3 (n=13) and abnormalities chr1 (n=10).

There was a strong correlation between the number of chromosomal abnormalities found in addition to abnormalities of chr17 and particular characteristics of the MDS patients (Table 2). There was a higher proportion of cases with monosomy 17 ($p<0.001$) and add17p ($p=0.008$) in the group with a

complex karyotype. The i(17q) was more frequent as an isolated abnormality or just with one associated anomaly ($p<0.001$).

No clear differences in demographic characteristics, variables used to calculate the IPSS, IPSS risk groups, and FAB and WHO classification were found between patients with loss or not loss of chr17p (17p-).

Outcome and prognostic factors in the patients with abnormalities of chr17

Sixty-six patients (75%) died during follow-up. Median OS was 9 months, with an actuarial risk of death of 47% at 6 months, 71% at 12 months, and of 78% at 24 months. In addition, 27 patients (31%) progressed to AML during the follow-up, with an actuarial risk of progression to AML of 19.3% at 12 months and 20.5% at 24 months.

The Table 3 shows the results of analyses of the different prognostic factors for OS and AML transformation in the patients with abnormality of chr17.

In relation to karyotype complexity for OS and risk of AML transformation, only two risk groups could be clearly identified: patients with an isolated chr17 abnormality or with one additional chromosomal abnormality and patients with two or more additional abnormalities (complex karyotype). Although patients with abnormality chr17 plus one additional abnormality had a somewhat shorter OS than patients with isolated abnormality chr17 the differences were not significant (median OS, 49 and 72 months, respectively; $p=0.81$). In contrast, patients with two or more additional abnormalities, in addition to chr17 anomaly, showed a much shorter OS (median OS, 5 mo) than the other two groups aforementioned groups ($p<0.001$ and $p=0.004$). Regarding the risk of

transformation to AML, the group with one additional abnormality had clearly lower risk than that of patients with a complex karyotype (median time to AML, 80 months versus 12.1 months; p = 0.008).

When analyzing the type of abnormality of chr17 we observed that cases with monosomy 17 had a worse prognosis in OS and transformation to AML than those with i(17q) (median OS, 6 versus 13 mo; p=0.011; median time to AML transformation, 10 versus 37 months; p=0.035 respectively). An isolated i(17q) was observed in 15 cases of the 29 cases with i(17q) (52%). The median OS for patients with isolated i(17q) was 29.8 months and 13.3% of them have transformed to AML.

The monosomy 17 also had a worse prognosis than a complex karyotype without monosomy 17 with a median OS of 6 and 9.7 months, respectively (p=0.001).

In the multivariate analysis we analyzed the prognostic impact concerning OS and AML transformation of karyotype complexity, monosomy of chr17 and isochromosome 17 as independent variables using the Cox regression model for survival data. The results showed that monosomy 17 and complex karyotype were independent prognostic factors for OS with a hazard ratio of 1,98 (IC95%: 1,10-3,59; p=0,023) and 4,52 (IC95%: 2,20-9,34; p<0,001) respectively. For AML transformation, only complex karyotype was found as an independent prognostic factor with a hazard ratio of 4,59 (IC95%: 1,58-10,43; p=0,004).

Comparison of OS and transformation to AML between patients with chr17 abnormality and patients with other chromosomal abnormalities not involving chr17

We compared data of OS and AML transformation of 88 patients with chr17 abnormalities with data of 1,346 patients with other chromosomal abnormalities not involving chr17 from the Spanish registry of MDS.

In Figure 1 we observed that patients with abnormalities of chr17 have a worse prognosis than patients with an abnormal karyotype without chr17 abnormalities for median OS (8.7 vs 30.0 mo respectively ($p < 0.001$)) and AML transformation (31% vs 22% respectively).

We compared the prognosis of the two groups of patients in each of the IPSS risk groups and IPSS cytogenetic risk groups (Table 4). In the IPSS Intermediate-2 risk group, patients with chr17 abnormality have a worse prognosis (median OS of 6.6 vs 14.0 mo in those without abnormality of chr17, $p=0.005$). In the IPSS cytogenetic risk groups of 1 point, the median OS of patients without abnormalities chr17 is of 29.1 months versus 11.9 months in patients with chr17 involved ($p < 0.001$).

In table 5 we summarize the results restricted to the group of patients with poor prognosis according to IPSS. The patients with monosomy of chr17 had a worse prognosis and higher probability to progression to AML than patients with isolated monosomy of chr7 (median OS of 4.7 vs 19.0 mo, $p<0.001$; and median time to AML transformation (MTT) of 9.8 vs 36.0 mo, $p=0.001$, respectively). Also, monosomy of chr17 was associated with a worse survival than patients with complex karyotype without chr17 abnormalities (median OS of 4.7 vs 8.0 mo, $p=0.015$).

In addition (Table 5), patients with i(17q), mainly with complex karyotype, have a worse prognosis in OS than patients with isolated monosomy of chr7 (median OS of 3.9 versus 19.0 mo, p=0.010). No statistical differences were found in survival or AML progression risk between patients with i(17q) and patients with complex karyotype not involving chr17.

DISCUSSION

In this paper we present the results of a multicenter cooperative study that recruited, in our knowledge, the largest to-date series of *de novo* MDS patients with abnormalities of chromosome 17. This has allowed us to assess the clinical characteristics and prognostic factors, with special emphasis on cytogenetic findings; being the survival and the risk of transformation to AML one of the highlights of this study.

According to the 1997 International Prognostic Scoring System (IPSS) (ref. 4) the abnormality of chr17 is grouped within the intermediate-risk cytogenetic group. Recently, the revised IPSS (IPSS-R) was published (ref. 25) and used the cytogenetic categories defined by Schanz et al (ref. 22) to stratify patients according five risk groups. In the proposal defined by Schanz et al., i(17)(q10) as a single anomaly was included in the intermediate risk category.

Our study aimed to characterize these patients with abnormality of chr17 and analyze whether we should continue to include them in the intermediate-risk cytogenetic group or if we need to consider chr17 alterations within groups of poor prognosis. This is one of the controversial points of the published studies about the IPSS-cytogenetic risk groups (ref. 8-12). Herein, we have studied extensively the characteristics and the outcome of patients with abnormality of chr17 and compared them with patients with chromosome abnormalities not involving chr17.

In our study, patients with abnormality of chr17 typically presented poor prognostic features (Table 1).

We found that patients with abnormalities of chr17 had a worse prognosis for OS and AML transformation than patients with abnormal karyotype but without

abnormalities of chr17. These results were found within the homogeneous intermediate-2 IPSS-risk group and 1 point IPSS cytogenetic group as well. When we analyzed the patients with complex karyotype, we found that if chr17 is involved, the prognosis is worsened.

Karyotype complexity is a well-known poor prognostic factor in MDS (ref. 4, 9, 11, 26-28). However, in MDS patients with anomaly of chr17 the prognostic value of the number of chromosomal abnormalities in addition to abnormality chr17 (complexity of the karyotype) has not been studied to date. We found two different prognostic groups of patients in function of number of chromosomal abnormalities: 1) patients with isolated abnormality of chr17 or with one associated abnormality and 2) patients with two or more associated abnormalities ($p<0.001$ and $p=0.004$ respectively).

The most frequent additional abnormalities to abnormality of chromosome 17 were: del(5q), followed by del(7q), monosomy 7, trisomy 8 and del(18q)/-18, the incidences of which were within the ranges reported in the literature (ref. 16, 29-34).

Concerning the type of abnormality of chr17 we showed that the i(17q) as an isolated alteration have a median OS of 29.8 months, slightly higher than the survival described in the new proposal for cytogenetic categorization of MDS (ref. 22) where the 11 patients with i(17q) had an intermediate prognosis with a median OS of 18 mo. About 70% of i(17q) were isolated or associated with just one abnormality and had better prognosis in OS and transformation AML than patients with monosomy 17 ($p = 0.011$ and $p = 0,035$). Regarding add(17p) seems to be a trend to worse prognosis in OS and transformation to AML respect to i(17q) without reaching statistical significance ($p=0.451$ and $p=0.852$).

This could be explained because patients with -17 or add(17p) present complex karyotype in the majority of cases ($p<0.001$ and $p=0.008$ respectively) and the i(17q) is usually as single abnormality or additional ones ($p<0.001$). However, at multivariate analysis we found that monosomy 17 is an independent prognostic factor. When i(17q), was included within a group of poor prognosis according IPSS, had a worse prognosis than patients with isolated monosomy 7 but no differences with complex karyotype without chr17 involved.

Regarding patients with monosomy of chr17, we found a worse OS and major risk of AML transformation than known subgroups of patients with bad prognosis according to IPSS (ref. 4), as -7 or complex karyotype. Several studies have shown in AML that the presence of autosomal chromosomal monosomies strongly predicted for an adverse prognosis. Negative prognostic impact of autosomal monosomies in AML has been described for monosomies of chromosomes 5 and 7 (ref. 35-37). However, according to the results, monosomy of chr17 should be considered as an additional worse prognosis factor in MDS patients and therefore, should support the possibility of a more upfront aggressive treatment when indicated.

Finally, we analyzed the characteristics and outcome of 72 patients fulfilling the "loss chr17p" definition. Comparing the OS and risk of evolution to AML of patients with the "loss chr17p" *vs* those "without loss chr17p" no significant differences were observed between both groups. Our work is based on the results of conventional cytogenetics (karyotype), it is a retrospective study and LOH17, TP53 loss or TP53 mutations could not be studied. These molecular studies would be very interesting to confirm with prospective specimens. Also, it

is interesting to note that i(17q) is usually presented as a single alteration and implies a 17q gain and 17p loss. If this were so, we might expect to find TP53 mutated and a different phenotype and prognosis. This should be demonstrated analyzing mutational status of TP53 by SNP arrays or sequencing. Taking this into account, the group of Houston studied the mutational status of TP53 in AML and other myeloid disorders with i(17q) and they did not find TP53 mutations (ref. 21) in any patient. In this regard it would be interesting to analyze TP53 mutational status in patients with MDS and i(17q).

A recent revision of the cytogenetic categorization of MDS has proposed five prognostic subgroups (ref. 22): very good, good, intermediate, poor and very poor prognosis with a median OS of 60.8, 48.5, 24, 14 and 5.7 months respectively. If we extrapolate the median survival of our patients with respect to that described by the IPSS-R (ref. 25), we may conclude that: the alterations of chr17 should be considered within group of poor prognosis (median OS 9 mo); i(17q) as an isolated disorder or with one additional alteration, may be included within the intermediate risk group (median OS 29.8); monosomy 17 has a much worse prognosis and we believe that these alterations should be included within the very poor prognosis group (median OS 6.2 mo). The rest of alterations of chr17 which include complex karyotype without monosomy 17 could be included into the poor prognosis group (median OS of 9.7 mo).

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Table 1

Table 1 Characteristics of the patients with abnormality of chr17

Characteristic	Number of patients, n (%)
Total number of patients	88
Age	88
< 60 years	9 (10.2)
≥ 60 years	79 (89.8)
Sex	88
Male	57 (64.8)
Female	31 (35.2)
Hemoglobin	87
< 10 g gr/dL	63 (72.4)
≥ 10 g gr/dL	24 (27.6)
Absolute neutrophil count	85
< 1.8 x 10^9 per liter	56 (65.9)
≥ 1.8 x 10^9 per liter	29 (34.1)
Platelet count	87
< 100 x 10^9 per liter	51 (58.6)
≥ 100 x 10^9 per liter	36 (41.4)
Cytopenias	86
0-1	23 (26.7)
2-3	63 (73.3)
BM blast count	88
< 5%	28 (31.8)
5-10%	24 (27.3)
11-19%	36 (40.9)
FAB subtype	88
RA	21 (23.9)
RARS	6 (6.8)
RAEB	61 (69.3)
WHO subtype*	84*
RA	3 (3.6)
RARS	3 (3.6)
RCMD	13 (15.5)
RCMD-RS	4 (4.7)
RAEB-1	24 (28.6)
RAEB-2	37 (44.0)
Karyotype complexity	88
Isolated abnormality chr17	18 (20.5)
Abnormality chr17 + 1 abnormality	8 (9.1)
Abnormality chr17 + 2 abnormality	5 (5.7)
Abnormality chr17 + 3 abnormality	9 (10.2)
Abnormality chr17 + ≥ 4 abnormality	48 (54.5)
Loss cr17p	88
Yes	72 (81.8)
Non	16 (18.2)
Chr17 type of anomaly	88
i (17q)	29 (33.0)
-17	26 (29.5)
add(17p)	13 (14.8)
+ 17	5 (5.7)
t 17	3 (3.4)
others	5 (5.7)
-17 and add(17p)	1 (1.1)
-17 and i(17q)	1 (1.1)
-17 and t 17	2 (2.3)
t17 and others	3 (3.4)
IPSS risk group	86
Low	0 (0)
Intermediate-1	19 (22.1)
Intermediate-2	35 (40.7)
High	32 (37.2)

Table 1: Characteristics of the patients with abnormality of chr17

Abbreviations: BM, bone marrow; FAB, French-American-British; IPSS, International Prognostic Scoring System; RA, refractory anemia; RAEB, RA with excess of blasts; RARS, RA with ringed sideroblasts; RCDM, refractory cytopenia with multilineage dysplasia; RCMD-RS, RCMD with ringed sideroblasts; WHO, World Health Organization; i(17q), isochromosome 17q; -17, monosomy chr17; add(17p), additional 17p; +17, trisomy cr17; t17, translocation chr17.
*In 4 patients WHO classification was not possible due to insufficient data.

Table 2

Table 2 Patient characteristics according to the karyotype complexity.

	isolated abnormality chr17 and abnormality chr17 + 1 abnormality		abnormality chr17 + ≥ 2 abnormalities		p value
	Median (Q1-Q3)	N (%)	Median (Q1-Q3)	N (%)	
Age < 60 years ≥ 60 years	72.98 (65-78.9)	26 3 (33.3) 23 (29.1)	73.34 (64.09-79.69)	62 6 (66.7) 56 (70.9)	0.793
Sex Male Female		26 21 (36.8) 5 (16.1)		62 36 (63.2) 26 (83.9)	0.042
Hemoglobin < 10 g gr/dL ≥ 10 g gr/dL	9.3 (8.4-10.4)	26 16 (25.4) 10 (41.7)	8.9 (7.8-9.8)	61 47 (74.6) 14 (58.3)	0.138
Absolute neutrophil count < 1.8 x 10^9 per liter ≥ 1.8 x 10^9 per liter	1.68 (0.8-2.37)	25 14 (25.0) 11 (37.9)	1.09 (0.61-2.33)	60 42 (75.0) 18 (62.1)	0.215
Platelet count < 100 x 10^9 per liter ≥ 100 x 10^9 per liter	113.5 (40-187)	26 12 (23.5) 14 (38.9)	60 (36-124)	61 39 (76.5) 22 (61.1)	0.123
Cytopenias 0-1 2-3		25 9 (39.1) 16 (25.4)		61 14 (60.9) 47 (74.6)	0.214
BM blast count < 5% 5-10% 11-19%	5.0 (3.0-10.0)	26 11 (39.3) 8 (33.3) 7 (19.4)	9.0 (4.0-14.0)	62 17 (60.7) 16 (66.7) 29 (80.6)	0.201
FAB subtype RA RARS RAEB		26 8 (38.1) 4 (66.7) 14 (23.0)		62 13 (61.9) 2 (33.3) 47 (77.0)	0.050
WHO subtype * RA + RARS RCMD + RCMD-RS RAEB-1 RAEB-2		25 2 (33.3) 9 (52.9) 7 (29.2) 7 (18.9)		59 4 (66.7) 8 (47.1) 17 (70.8) 30 (81.1)	0.090
IPSS risk group Intermediate-1 Intermediate-2 High		26 15 (78.9) 7 (20.0) 4 (12.5)		60 4 (21.1) 28 (80.0) 28 (87.5)	<0.001
Loss chr17p Yes Non		26 21 (29.2) 5 (31.2)		62 51 (70.8) 11 (68.8)	0.869
Chr17 type of abnormality** i (17q) -17 add(17p) trisomy 17 traslocation 17		24 20 (69.0) 1 (3.8) 0 (0) 3 (60.0) 0 (0)		52 9 (31.0) 25 (96.2) 13 (100) 2 (40.0) 3 (100)	<0.001 <0.001 <0.001 0.008 0.124 0.055

Table 2: Patient characteristics according to the karyotype complexity.

Abbreviations: BM, bone marrow; FAB, French-American-British; IPSS, International Prognostic Scoring System; RA, refractory anemia; RAEB, RA with excess of blasts; RARS, RA with ringed sideroblasts; RCDM, refractory cytopenia with multilineage dysplasia; RCMD-RS, RCMD with ringed sideroblasts; WHO, World Health Organization. Q1, percentile 25; Q3, percentile 75.

* In 4 patients WHO classification was not possible due to insufficient data.

** Other abnormalities and associations of two abnormalities of chr17 not shown. Each subtype is compared with the presence or absence the abnormality between the group of karyotype complexity.

Table 3

Table 3 Results of analyses of prognostic factors for OS and AML transformation in the patients with abnormality of chr17

	Overall survival				AML transformation			
	N (%)	Median survival (mo)	Patients alive at 1 year (%)	p value	N (%)	Median AML transformation (mo)	Patients transformed in AML (%)	p value
Age	88 (100)			0.053	27 (30.6)			0.652
< 60 years	9 (10.2)	12.2	44.4		4 (14.8)	36.5	44.4	
≥ 60 years	79 (89.8)	8.1	27.8		23 (85.2)	29.4	29.1	
Sex	88 (100)			0.474	27 (100)			0.301
Male	57 (64.8)	9.1	28.1		15 (55.5)	33.1	26.3	
Female	31 (35.2)	6.2	32.3		12 (44.5)	27.0	38.7	
Hemoglobin	87 (98.8)			0.121	27 (100)			0.465
< 10 gr/dL	63 (71.6)	7.3	25.4		15 (55.5)	34.6	23.8	
≥ 10 gr/dL	24 (27.3)	12.2	41.7		12 (44.5)	29.4	50.0	
Absolute neutrophil count	85 (96.5)			0.919	27 (100)			0.812
< 1.8 x 10^9 per liter	56 (63.6)	9.0	25.0		17 (62.9)	32.0	30.4	
≥ 1.8 x 10^9 per liter	29 (33.0)	8.5	37.9		10 (37.1)	33.1	34.5	
Platelet count	87 (98.8)			0.007	27 (100)			0.129
< 100 x 10^9 per liter	51 (58)	7.5	21.6		15 (55.5)	27.0	29.4	
≥ 100 x 10^9 per liter	36 (40.9)	27.1	41.7		12 (44.5)	36.5	33.3	
Cytopenias	86 (97.7)			0.068	27 (100)			0.809
0-1	23 (26.7)	20.9	47.8		11 (40.7)	33.1	47.8	
2-3	63(73.3)	7.5	22.2		16 (59.3)	32.0	25.4	
BM blast count	88 (100)			0.205	27 (100)			0.168
< 5% (1)	28 (31.8)	12.2	39.3	(1) vs (2) 0.046	7 (25.9)	34.6	25	(1)vs(2)0.094
5-10% (2)	24 (27.3)	6.8	16.7	(1)vs(3) 0.201	6 (22.2)	12.1	25	(1)vs(3)0.075
11-19% (3)	36 (40.9)	7.3	30.6	(2) vs (3) 0.628	14 (51.9)	27.4	38.9	(2)vs(3)0.921
FAB subtype	88 (100)			0.110	27 (100)			0.063
RA + RARS	27 (30.7)	12.2	44.4		7 (25.9)	34.6	25.9	
RAEB	61 (69.3)	7.3	23.0		20 (74.1)	27.0	32.8	
WHO subtype	84 (95.4)			0.312	27 (100)			0.232
RA + RARS (1)	6 (7.6)	36	83.3	(1)vs(2) 0.210	2 (7.5)	79.9	33.3	(1)vs(2) 0.051
RCMD + RCMD-RS (2)	17 (21.7)	12.0	35.3	(1)vs(3) 0.022	5 (18.5)	32.0	29.4	(1)vs(3) 0.141
RAEB-1 (3)	24 (27.2)	6.8	16.7	(1)vs(4) 0.125	5 (18.5)	---*	20.8	(1)vs(4) 0.049
RAEB-2 (4)	37 (41.3)	7.3	27.9	(2)vs(3) 0.280	15 (55.5)	27.0	40.5	(2)vs(3) 0.630
				(2)vs(4) 0.501				(2)vs(4) 0.575
				(3)vs(4) 0.815				(3)vs(4) 0.575
IPSS risk group	86 (97.7)			0.025	27 (100)			0.050
Intermediate-1 (1)	19 (21.6)	36	62.2	(1) vs (2) 0.007	6 (22.2)	79.9	31.6	(1) vs (2) 0.090
Intermediate-2 (2)	35 (39.8)	6.6	17.1	(1) vs (3) 0.007	8 (29.6)	29.4	22.9	(1) vs (3) 0.008
High (3)	32 (36.4)	6.2	25.0	(2) vs (3) 0.955	13 (48.2)	10.0	40.6	(2) vs (3) 0.576
karyotype complexity	88 (100)			<0.001	27 (100)			0.008
Isolated abnormality chr17 (1)	18 (20.4)	71.8	61.1	(1) vs (2) 0.808	4 (14.8)	---*	22.2	(1) vs (2) 0.739
Alt. chr17 + 1 abnormality (2)	8 (9.0)	48.7	55.6	(1) vs (3) <0.001	3 (11.1)	79.9	37.5	(1) vs (3) 0.007
Abnormality chr17 + ≥ 2 abnormalities (3)	62 (70.5)	5.4	16.4	(2) vs (3) 0.004	20 (74.1)	12.1	32.3	(2) vs (3) 0.068
Type of abnormality chr17	76 (86.3)			0.018	27 (100)			0.125
i(17q) (1)	29 (33.0)	13.4	48.3	(1) vs (2) 0.011	8 (29.6)	36.8	27.6	(1) vs (2) 0.035
-17 (2)	26 (29.5)	6.2	11.5	(1) vs (3) 0.451	11 (40.7)	9.8	42.3	(1) vs (3) 0.852
add(17p) (3)	13 (14.8)	12.0	30.8	(2) vs (3) 0.206	4 (14.8)	34.9	30.8	(2) vs (3) 0.056
Loss cr17p	88 (100)			0.233	27 (100)			0.291
Yes	72 (81.8)	8.1	39.2		23 (85.2)	29.4	31.9	
Non	16(18.2)	9.7	31.3		4 (14.8)	79.9	25	

Table 3: Results of analyses of prognostic factors for OS and AML transformation in the patients with abnormality of chr17

Abbreviations: AML, acute myeloid leukemia; BM, bone marrow; FAB, French-American-British; IPSS, International Prognostic Scoring System; RA, refractory anemia; RAEB, RA with excess of blasts; RARS, RA with ringed sideroblasts; RCDM, refractory cytopenia with multilineage dysplasia; RCMD-RS, RCMD with ringed sideroblasts; WHO, World Health Organization.
* median not reached

Table 4

Table 4 Results OS between patients with abnormality of chr17 vs without abnormality of chr17 for each IPSS risk-group.

		Overall survival				
		Abnormality of chr17		No abnormality of chr17*		p value
		N	MST	N	MST	
IPSS risk group	Intermediate-1	19	36.3	508	42.0	0.134
	Intermediate-2	35	6.7	300	14.0	0.005
	High risk	32	6.3	227	8	0.644
IPSS cytogenetic group	0.5	25	60.3	526	54.3	0.229
	1	63	11.9	358	29.1	<0.001

Table 4 Legend

Table 4: Results OS between patients with abnormality of chr17 vs without abnormality of chr17 for each IPSS risk-group.

* Patients with a low IPSS risk group and 0 points of the IPSS cytogenetic group not shown.
MST (Median OS);

Table 5

Table 5 OS and AML transformation in high risk-group of IPSS according to type of alteration of crh17.

		Overall survival			AML transformation		
	N	MST (mo)	Exitus (%)	p value	MTT (mo)	Patients transformed in AML (%)	p value
Monosomy of cr17 (1)	25	4.7	88.0	(1) vs (3) <0.001	9.8	40.0	(1) vs (3) 0.001
Isochromosome of cr17 (2)	10	3.9	100.0	(1) vs (4) 0.015	---**	40.0	(1) vs (4) 0.084
Monosomy of cr7 (3)	56	19.0	64.3	(2) vs (3) 0.010	36.0	26.8	(2) vs (3) 0.110
Complex karyotype* (4)	234	8.0	79.5	(2) vs (4) 0.183	16.0	34.2	(2) vs (4) 0.310

Table 5 Legend

Table 5: OS and AML transformation in high risk-group of IPSS according to type of alteration of crh17.

* Patients with complex karyotype involving abnormalities of chr7 and chr17 not included
** MTT not reached
MST (Median OS); MTT (median time to AML transformation)

Figure 1

Figure 1: Compared data of OS and LAM transformation of patients with chr17 abnormalities with patients with other chromosomal abnormalities not involving chr17.

Figure 1A

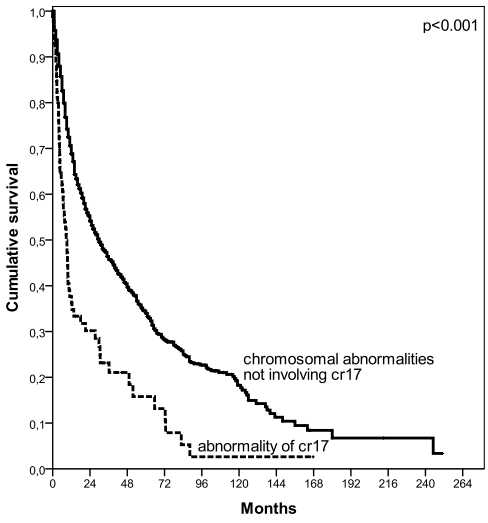

Figure 1B