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To the editor:

The impact of abn(17p) and monosomy –5/del(5q) on the prognostic value of the monosomal karyotype in acute myeloid leukemia

Acute myeloid leukemia (AML) with monosomal karyotype (MK) at diagnosis has been established as a subset of AML patients with very poor prognosis. After the initial publication by the Dutch-Belgian Hemato-Oncology Cooperative Group and Swiss Group for Clinical Cancer Research (HOVON/SAKK),¹ several studies confirmed the very unfavorable prognostic significance of AML-MK.^{2,3} Recently, Middeke et al⁴ reported that MK and complex karyotypes in AML lost their excessively poor prognostic value after allogeneic stem cell transplantation (SCT) when AML with abn(17p) or –5/del(5q) were excluded from the AML-MK or AML-complex karyotypes subcategories. Although the impact of abn(17p) or –5/del(5q) among MK was also studied in our original publication,¹ the prognostic distinction that was proposed by Middeke et al was not apparent in our analysis. We set out to examine whether we could confirm the observations of Middeke et al in an expanded cohort of 2898 newly diagnosed AML patients 15 to 60 years of age entered into 5 successive HOVON/SAKK trials between 1987 and 2008.⁵⁻⁹

From those 2898 patients, patients with normal karyotype, core binding factor abnormalities, or sole –X or –Y were not considered

in this regard so that 1109 patients with ≥1 other chromosomal abnormalities were included in the analysis. Among this latter group, 305 patients had AML-MK. We estimated overall survival (OS) and event-free survival (EFS) of patients with AML-MK and MK subgroups with or without abn(17p) or –5/del(5q) (Table 1). Patients with AML-MK with –5/del(5q) showed an extremely unfavorable 3-year OS from diagnosis (2%), whereas AML-MK patients without –5/del(5q) showed statistically significant better but still very poor 3-year OS (12%), which is much less than the OS of non-MK patients. The same trend was seen in the subgroup of patients with AML-MK after allogeneic SCT in first complete remission, although with reduced statistical significance. The presence or absence of abn(17p) among AML-MK patients showed no relation whatsoever with OS and EFS after diagnosis or after allogeneic SCT and thus did not add prognostic value. Because the various studies spanned a time period that was >20 years and the 5-year OS and EFS improved from 29% and 22% for patients diagnosed between 1987 and 1993 to 43% and 35% for patients diagnosed after 2003, a multivariate regression analysis adjusted for the year of diagnosis was performed. The *P* values from this

Table 1. Overall survival and event-free survival of AML-MK at 3 years after diagnosis and after allogeneic stem cell transplantation in AML-MK in relation to the specific cytogenetic abnormalities abn(17p) or –5/del(5q)

Chromosomal abnormality	After diagnosis			After allogeneic stem cell transplantation		
	No.	OS (SE) at 3 y	EFS (SE) at 3 y	No.	OS (SE) at 3 y	EFS (SE) at 3 y
MK total	305	7 (1)	5 (1)	49	28 (6)	26 (6)
With abn(17p)	38	5 (4)	5 (4)	7	29 (17)	29 (17)
Without abn(17p)	267	7 (2) <i>P</i> = .90	6 (1) <i>P</i> = .79	42	28 (7) <i>P</i> = .93	25 (7) <i>P</i> = .81
With –5/del(5q)	172	2 (1)	2 (1)	25	16 (7)	11 (7)
Without –5/del(5q)	133	12 (2) <i>P</i> < .01	10 (3) <i>P</i> = .02	24	41 (10) <i>P</i> = .06	41 (10) <i>P</i> = .03
Non-MK abnormalities	804	35 (2)	25 (2)	223	54 (3)	51 (3)

AML patients with normal karyotypes, core binding factor abnormalities, or sole –X or –Y were excluded. Non-MK abnormalities refers to AML not meeting the definition MK but with other non-core binding factor cytogenetic abnormalities as previously described.¹
SE, standard error.

analysis were virtually identical to those from the unadjusted analysis shown in Table 1.

Thus, in contradiction with the report of Middeke et al,⁴ in this large analysis, MK holds its notoriously adverse prognostic value and does not depend on the inclusion of AML patients with *abn(17p)* and *-5/del(5q)*. Allogeneic SCT has a positive effect on the survival probabilities of patients with AML-MK and is regarded as the preferred treatment option for these patients.¹⁰ Nevertheless, in the current analysis, allogeneic SCT recipients with AML-MK still show a relatively unfavorable outcome compared with transplant recipients with AML with other non-core binding factor chromosomal abnormalities (Table 1), although the presence of *-5/del(5q)* apparently exerts some additional negative prognostic effect. In conclusion, we cannot confirm that the exclusion of *abn(17p)* or *-5/del(5q)* from the MK abolishes the strong negative prognostic impact of AML-MK.

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