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**Acute Myeloid Leukemia**

**Limited value of FLT3 mRNA expression in the bone marrow for prognosis and monitoring of patients with acute myeloid leukemia**

We studied wild-type FLT3 mRNA expression at diagnosis in bone marrow samples from 85 patients with acute myeloid leukemia (AML), 23 of whom were in complete remission, and determined its utility as a marker for minimal residual disease (MRD). We conclude that FLT3 expression is of limited value as a prognostic marker and for MRD monitoring.

**Table 1. Clinical characteristics and laboratory parameters of the 85 patients.**

<table>
<thead>
<tr>
<th>FLT3 mRNA expression (median)</th>
<th>Sex</th>
<th>Age (median)</th>
<th>WBC (median)</th>
<th>LDH (median)</th>
<th>BM blasts</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.09-fold</td>
<td>M=38 (45%)</td>
<td>57 years</td>
<td>27.2×10^9/L</td>
<td>385 U/L</td>
<td>74%</td>
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<tr>
<th>FLT3-ITD: n=77</th>
<th>FLT3-ITD+</th>
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<td>16 (21%)</td>
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*p values are not significant unless indicated. p<0.05. Associations between FLT3, mRNA expression and clinical and laboratory parameters are described by Spearman’s correlation. Data analysis was performed using WinStat for Windows (1995 Version 3.3). For cytogenetic analysis, 15-20 metaphases were analyzed. The definition of high, intermediate and low risk groups was that of the MRC AML 10 Trial.*

 FLT3, expressed in the blast cells in a majority of patients with acute myeloid leukemia (AML), is a novel therapeu-
tic target and might be a candidate for minimal residual disease (MRD) monitoring. Only a few studies are available regarding FLT3 mRNA expression in leukemic cells in AML patients, and to our knowledge this is the first report concerning the use of FLT3 mRNA expression for MRD monitoring. Eighty-five non-consecutive previously untreated adult AML patients were studied in this retrospective analysis. Their clinical characteristics are given in Table 1. The diagnosis of AML was established according to FAB criteria. Induction therapy was daunorubicin 45 mg/m² days 1-3, etoposide 100 mg/m² days 1-5, and cyto-
sine arabinoside 2×100 mg/m² days 1-7 (n=79) and ATRA-containing chemotherapy for M3 patients (n=6). Fifteen patients underwent allogeneic stem cell transplantation in first complete remission (CR). Real-time polymerase chain reaction (PCR) from cDNA from unsorted frozen bone marrow (BM) or peripheral blood mononuclear cells was performed with the ABI Prism 7000 Sequence Detector (Applied Biosystems (AB)) according to the manufacturer’s instructions with FLT3-specific primers (AB, Assay ID: Hs00174690). β-actin (AB, pre-developed VIC™-labeled TaqMan™ Assay) was used as an endogenous control. Delta values were calculated as the difference between CT (threshold cycle) values (∆CT=CT(ITUl)-CT(β-actin)). Material for FLT3-ITD detection was available for 77/85 patients; FLT3-ITD assessment was performed as previously described.

Of 4 patients staged for lymphoma without BM involvement was used as a control. Mean FLT3 mRNA expression in these samples was taken as having a value of 1. FLT3 mRNA was overexpressed in 84 of 85 patients (range 0.6- to 214-fold, median 22.09-fold) in comparison to our controls.

We found that high FLT3 expression correlated with a high percentage of BM blasts (p=0.002) and FAB classification (M5 was associated with low and M1 with high expression, p=0.002 and p=0.04, respectively). Regarding clinical parameters, we found no correlation with cytogenetic risk groups, white blood count and serum lactate dehydrogenase, but a skewed sex distribution with higher expression in males. Expression levels were higher in patients with FLT3-ITD, but the difference was not statis-

Letters to the Editor

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expression from diagnosis to CR was not significantly different between the CCR and the relapse group (Figure 1).

We show that FLT3 mRNA is overexpressed in almost all patients with AML, but the degree of overexpression in diagnostic BM samples has no influence on OS. A good marker for MRD monitoring should decrease by more than 3 logs in CR, which was never the case in our group of patients, because the background expression in normal bone marrow was too high to allow for sensitive detection of MRD. FLT3 Therefore, we suggest that the usefulness of FLT3 expression as a marker for MRD is limited.

At diagnosis Complete Normal remission bone marrow

Figure 1. FLT3 expression in patients in CCR and relapsed patients at diagnosis and at time of remission. At diagnosis the patients showed a median 26.9-fold (CCR patients) or 21.9-fold (relapsed patients) FLT3 overexpression compared to normal bone marrow (normal bone marrow expression=1). In CR the expression decreased to a mean of 2.1-fold (CCR patients) or 1.4-fold (relapsed patients) higher than in normal bone marrow.