CORRESPONDENCE

NO CORRELATION BETWEEN THE TYPE OF bcr-ab1 HYBRID MESSENGER RNA AND PLATELET COUNTS IN CHRONIC MYELOGENOUS LEUKEMIA

To the Editor:

The consistent genetic marker of chronic myelogenous leukemia (CML) is the Philadelphia translocation t(9;22), resulting in formation of a hybrid bcr-ab1 gene and expression of the fusion protein p210[br]. The breakpoints on chromosome 22 are clustered within a stretch of 5.8 kbp, the major breakpoint cluster region (M-bcr), harboring four small exons, b1 through b4. On the basis of restriction sites, the breakpoints within the M-bcr can be mapped 5' or 3' to a central HindIII site downstream of M-bcr exon b3. Dependent on the localization of the breakpoint and/or differential splicing, exon b3 is part of the chimeric bcr-ab1 messenger RNA (b3a2 type) or is not (b2a2 type).

Recently, a correlation between location of the breakpoint or the type of bcr-ab1 mRNA and platelet counts was described. We have analyzed bcr-ab1 mRNA by cDNA-polymerase chain reaction (PCR) in peripheral blood or bone marrow samples of 45 patients with Philadelphia chromosome-positive CML. An example of an agarose gel resolving the different amplification products is shown in Fig 1. Twenty patients expressed the b3a2 mRNA, 15 the smaller b2a2 transcript, and 10 patients showed both types. Minor amounts of the b2a2 or b3a2 transcripts were found in single samples of patients expressing mainly b3a2 or b2a2 mRNA, respectively (eg, see patient 4 in Fig 1). These patients were typed according to the predominant species and are marked in Fig 2. Statistical analysis was performed, including and excluding these patients. In Fig 2 the platelet counts of the 45 patients are given. The median platelet counts were 377 x 10^9/L (range 120 to 1,600) for patients with b3a2 transcripts, 303 x 10^9/L (range 117 to 1,868) for patients with b2a2 transcripts, and 418 x 10^9/L (range 188 to 1,000) for those patients expressing both transcripts. These differences are far away from significance (P value .6042). When the patients with spurious amounts of the second transcripts as indicated in Fig 2 were omitted, the P value was .5211. Thus, in contrast to the reports of Inokuchi et al and Lee et al, we cannot find an enhanced thrombopoietic potential in patients carrying exon b3. It should be noted that only 10 of the patients reported here are included in our investigation comparing genomic breakpoints and platelet counts, giving no significant differences as well. Thus, we have scored a total of 88 patients without evidence for correlation of genomic break region or mRNA type and platelet counts.

A comparison of type of mRNA and hemoglobin levels or leukocyte counts at diagnosis showed no significant differences with P values of .0859 (.0777) and .2301 (.3757), respectively. The values in brackets are calculated omitting the patients with minor expression of the other type of mRNA as indicated in Fig 2. This is not discussed further.}

![Fig 1. An ethidium bromide-stained 2.5% agarose gel is shown resolving products of bcr-ab1-specific cDNA PCR. The PCR products representing the b3a2 and b2a2-type mRNAs are marked. The numbers identify individual patients' samples, in lane 12 cDNA of the CML cell line K562 is shown as positive control. Patient 4 expresses mainly b2a2 mRNA and a very low amount of b3a2 mRNA, patients 3 and 6 express both transcripts simultaneously. HaeIII digested φX174 DNA was used as a size marker. Fragment sizes are given in base pairs (bp).](image-url)
In conclusion, our data do not support clinical relevance of presence or absence of M-bcr exon b3 in the mRNA of CML patients.

ACKNOWLEDGMENT

Supported by the Wilhelm Sander Foundation. We thank U. Roggenbuck for help with statistics, M. Kranzhoff for secretarial help, and N. Lobbenmeier for technical assistance.

BERTRAM OPALKA
Institute of Molecular Biology

URSULA B. WANDL

RUTH STUTENKEMPER

OTTO KLOKE

SIEGFRIED SEEBER

Department of Internal Medicine
(Cancer Research)

West German Cancer Center Essen
University of Essen Medical School

NORBERT NIEDERLE

Department of Internal Medicine III
Städt. Krankenhaus
Leverkusen, Germany

REFERENCES


No correlation between the type of bcr-abl hybrid messenger RNA and platelet counts in chronic myelogenous leukemia [letter]

B Opalka, UB Wandl, R Stutenkemper, O Kloke, S Seeber and N Niederle