

R.A. Stark
L. Wright
J.C. Biggs
P.P. Kearney

The bcr Breakpoint and Chronic Phase Duration in Chronic Myeloid Leukaemia

Allogeneic bone marrow transplantation is the only proven cure for chronic myeloid leukaemia (CML). The timing of bone marrow transplantation in individual patients can be difficult although clinical variables may provide some guide to urgency [1]. The oncogenic events underlying the Philadelphia chromosome are now well described and molecular variations may also have prognostic significance. Several groups have suggested that the position of the bcr breakpoint may influence the chronic phase duration; however, these findings have not been confirmed by other authors [reviewed in ref. 2]. One variable hindering comparison of these studies has been the different methods used to examine the bcr breakpoint position. Using the methods of Mills et al. [3], and probes kindly provided by these authors, the bcr breakpoint position was determined in 40 patients with CML. Table 1 compares patients with 5' and 3' bcr breakpoints. The chronic phase duration was not significantly different between the two groups ($p = 0.122$). The distribution of breakpoints by zone was similar to that previously described [2]. These findings do not confirm the conclusions of Mills et al. [3] that the chronic phase duration in CML is shorter in pa-

Table 1. Comparison of CML patients with 5' and 3' bcr breakpoints

	5' breakpoint		3' breakpoint	
Patients, n	26		14	
Mean age, years	36.9		39.6	
Sex (M:F)	11:15		8:6	
Chronic phase duration, months	30		38	
Zone of bcr breakpoint	1 or 2	3	4	5
Patients, n	6	20	11	3

tients with 3' bcr breakpoints. This is despite the fact that we have used identical methods and probes as these authors. We agree that patient variables may explain the different conclusions of these studies and that a long-term prospective study may be required to resolve this controversy. Included in this study is a patient with an exceptionally long chronic phase (20 years); molecular analysis revealed a zone 5 (3') breakpoint. Such patients suggest that oncogenic events unrelated to bcr-abl are involved in the progression of CML.

References

- 1 Sokal JE, Baccarini M, Tura S, et al: Prognostic discrimination among younger patients with granulocytic leukaemia; Relevance to bone marrow transplantation. *Blood* 1985;66:1352.
- 2 Mills KI, Benn P, Birnie GD: Does the breakpoint within the major breakpoint cluster (M-bcr) influence the duration of the chronic phase in chronic myeloid leukemia? An analytic comparison of current literature. *Blood* 1991;78:1155.
- 3 Mills KI, MacKenzie ED, Birnie GD: The site of breakpoint within the bcr is a prognostic factor in Philadelphia-positive CML patients. *Blood* 1988;72:1237.