To the Editor:

The letter from Kurosawa et al. draws attention to the phenomena of changing p53 mutation status with the clinical progression of chronic myeloid leukemia (CML) from the chronic phase to blast crisis that we have also observed. Infrequent cases of p53 mutations in the chronic phase have been reported and a changing p53 status in the blast crisis of CML with patient treatment has been described previously.

We postulate that part of the mechanism of clonal evolution in these CML patients has been elicited by our study and by other studies. We propose that the late chronic-phase p53 mutant clones in our study were removed by chemotherapeutic treatment to below the level of detection by the PCR-SSCP technique. In the meantime, a different p53 abnormal clone evolved that was resistant to treatment, expanded, and was evident in the blast crisis that followed. The same chronic-phase p53 abnormality was also found at bone marrow transplant relapse. Similar findings have also been described in blast crisis samples from a CML patient.

Several groups have found p53 mutations in the late chronic phase of CML and the genomic evolution of multiple clones seen, by virtue of changing p53 status in CML, has been described previously. The detection of p53 mutations in the late chronic phase may be an indicator of increasing genomic instability and imminent progression to blast crisis.

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REFERENCES

p53 mutations indicate a changing clonal evolution in a portion of chronic myelocytic leukemia patients [letter; comment]

BA Guinn, RA Padua, A Burnett and K Mills