Detection of Minimal Residual Disease in Acute Leukemia

To the Editor:

Campana and Pui have failed to mention in their well-balanced and lucid review article on minimal residual disease (MRD) in leukemia two important practical aspects of quantitating MRD by polymerase chain reaction (PCR). First, the quantitation of MRD by PCR is not precise, and the method based on Poisson statistics used by Brisco et al. is no exception. If MRD quantitation were to be performed on the same sample on different days, up to twofold difference in the amount of MRD may be observed. This poor reproducibility should be kept in mind before changing treatment based on the detection of MRD. Second, the method of preparation of the remission bone marrow for DNA extraction may also influence the amount of MRD detected. For example, the PCR method is likely to amplify target genes from DNA released from dead cells (not clonogenic). The time taken for the bone marrow to remove the dead leukemic cells may be variable depending on the initial leukemic load and the ability of the reticuloendothelial system to remove the debris. DNA prepared from a buffy coat preparation or a whole bone marrow suspension is more likely to contain DNA from dead cells as opposed to DNA prepared from, e.g., Hypaque-Ficoll-separated bone marrow cells.

These two practical issues may explain the wide variations in the reported percentage of patients with MRD at the time of initial remission (around 6 weeks from diagnosis) and might partly explain the observation that the percentage of patients with detectable MRD is lower in studies reporting MRD after several months from diagnosis. These practical issues must be addressed in prospective studies designed to validate the prognostic importance of MRD in acute leukemia. It is premature to intensify therapy in patients with a high amount of MRD at the time of initial remission and to decrease therapy in patients with no detectable MRD. It must be kept in mind that prognosis in leukemia is relative to the treatment and that good results obtained in patients with no MRD may be because of the currently available therapy, which is better than the therapy used 2 decades ago. To change the current practice in good prognosis patients may be an invitation for disaster.

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REFERENCES

Expression of HLA-DR (major histocompatibility complex class II) on neutrophils from patients treated with granulocyte-macrophage colony-stimulating factor for mobilization of stem cells [letter]

SP Mudzinski, TP Christian, TL Guo, E Cirenza, KR Hazlett and EJ Gosselin