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Detection of minimal residual disease (MRD) by flow cytometry in children with acute lymphoblastic leukemia (ALL)

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Abstract

Background: The initial response of leukemia cells to treatment has consistently been shown to be a reliable prognostic indicator, and its evaluation has been significantly enhanced by methods that allow detection of submicroscopic levels of leukemia.

Methods: From January 2007 to April 2009, 45 patients with newly-diagnosed ALL were enrolled in ALL-IC BFM 2002 studies at our institution and had residual disease studies by flow cytometry on day 15 and day 33 of treatment. Of the 45 patients, 37 patients (82.2%) had a BCP-ALL and 8 had T-ALL (17.8%). Analyses were performed on a FACScan (Becton Dickinson). We used several standardized antibody combinations to screen ALL samples at diagnosis for leukemia-associated aberrations as well as to investigate BM.

Results: In 40 samples (88.9%) on day 15 we identified at least 0.01% leukemic cells (0.01%–<0.1% in 12 (26.7%), 0.1%–<1% in 16 (35.6%), and ≥1% in 12 (26.7%). Of the 45 bone marrow samples studied by flow cytometry on day 15 of remission–induction therapy, 11 (24.4%) had leukemic lymphoblasts identifiable by morphologic analysis. In all the 11 morphologically positive samples, at least 0.1% cells expressing leukemia-specific immunophenotypes were detected by flow cytometry (median 17.2%, range 0.37% to 82.2%). Among the 34 (75.6%) samples without leukemic lymphoblasts recognizable by their morphologic features, 29 (64.5%) had detectable cells expressing leukemia-associated immunophenotypes (median 1.4%, range 0.01% to 25%).

Conclusion: The proportion of samples that were MRD^+ was high on day 15 and decreased to 59.6% on day 33. Children with ALL who achieved an early clearance of leukemic cells had an excellent outcome.

Keywords: acute lymphoblastic leukemia, children, minimal residual disease, flow cytometry