normal bone marrow cells (253). In commentary on ALL, Pui (254) finds that MRD levels on day 15 were a powerful prognostic factor.

In commentary on acute promyelocytic leukemia (APL), Grimwade et al. (255) found that MRD monitoring successfully identified most patients subject to relapse and provided a powerful predictor of relapse-free survival (RFS). Thus, MRD is sometimes used as a surrogate endpoint in the hematological cancers, though the utility of MRD differs depending on the cancer (256,257,258).

MRD test results have the following utilities. Grimwade et al. (259) and Campana (260) find that MRD measurements can provide the risk of relapse, direct pre-emptive therapy, guide the selection of intensity and duration of treatment, and provide guidance for treatment of the leukemia with stem cell transplantation.

a. Example of use of minimal residual disease and relapse – the Scheuring study of Philadelphia chromosome positive ALL

In a study of ALL (Ph positive ALL), Scheuring et al. (261) acquired samples of PBMCs and bone marrow immediately before chemotherapy, and after 2 weeks, after 4 weeks, and at monthly intervals thereafter. The authors determined the date of minimal residual disease. Because of the repeated samplings of PBMCs, they were able to determine the date when there occurred a significant increase in blasts in the PBMC sample. This date was then compared to the date of relapse and graphed on the Kaplan-Meier plot. Relapse was defined as the reappearance of blasts in the PBMCs in a patient and where that patient had earlier achieved a reduction in bone marrow blasts to less than 5% with no detectable blasts in the PBMCs.

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