



Figure 17.3 Schematic diagram of Kaplan-Meier plot of ALL. The plot shows the percentage of all subjects (X axis) versus time from date of significant increase in blasts until date of relapse. The upper curve corresponds to subjects with a low increase in MRD, while the lower curve corresponds to subjects with a high increase in MRD

The schematic diagram of the Kaplan-Meier plot (Fig. 17.3) shows the proportion of patients, during the time course of the clinical trial, experiencing relapse. Two curves are shown in the Kaplan-Meier plot. The upper curve corresponds to subjects with a relatively low increase in MRD (when the increase was first detected), while the lower curve corresponds to subjects with a relatively high increase in MRD (when the increase was first detected). The authors discovered that, in assays of PBMC blasts, an increase that was under 5×10^{-4} was associated with a longer time to relapse, while an increase above 5×10^{-4} was associated with a shorter time to relapse (median 27 days to relapse) (Fig. 17.3).

The authors concluded that this assay method enabled detection of patients with poor prognosis and in need of more aggressive therapy.

b. Example of use of minimal residual disease and event-free survival – the Basso study of Philadelphia chromosome negative ALL

In a study of childhood ALL (Ph negative ALL), Basso et al. (262) stratified patients according to minimal residual disease (MRD) data that were collected from bone marrow samples on day 15 of the study. The MRD data were combined with established cytogenetics parameters, and this combination was used to define the following risk groups:

- 1. High risk.** $t(4;11)(q21;q23)$ or MLL/AF4, and testing positive for MRD, where blast counts were greater or equal to 10%. MLL/AF4 refers to the fusion of MLL gene and AF4 gene, a fusion product often found in infant ALL. The MLL gene is also known as ALL1, HRX, and Hrx1(263).

²⁶² Basso G, Veltroni M, Valsecchi MG, et al. Risk of relapse of childhood acute lymphoblastic leukemia is predicted by flow cytometric measurement of residual disease on day 15 bone marrow. *J Clin Oncol.* 2009;27:5168–5174.

²⁶³ Cimino G, Cenfra N, Elia L, et al. The therapeutic response and clinical outcome of adults with ALL1(MLL)/AF4 fusion positive acute lymphoblastic leukemia according to the GIMEMA experience. *Haematologica.* 2010;95:837–840.