Table 17.5 Response of CLL patients to fludarabine alone or to fludarabine plus cyclophosphamide

	Objective response (complete response; CR)	Progression-free survival (PFS)
Fludarabine alone	5.3%	19.9 months
Fludarabine plus cyclophosphamide	24.6%	33.5 months

baseline from each patient, that is, before administering any drugs. Two hundred cells (PBMCs) were evaluated using each fluorescent probe, and the results were expressed as the percentage of nuclei with an abnormal signal pattern for any probe and corresponding chromosomal anomaly. Cytogenetic analysis was by the technique of fluorescence in situ hybridization (FISH), using methods suited for chronic lymphocytic leukemia (CLL) (246).

For the purposes of cytogenetic analysis, survival data from all 235 subjects were pooled, and then separated into three different curves. The three curves appear in a Kaplan-Meier plot in the original journal article. The three curves did not correspond to different treatments, but instead they corresponded to the cytogenetics of the leukemia. Thus, the three different curves corresponded to subjects where blood cells contained: (1) the del(17p13.1) chromosomal abnormality; (2) the del(11q22.3) chromosomal abnormality; and (3) other chromosomal abnormalities. The results were as follows. The median PFS was 10.8 months for patients with del(17p13.1) and 21.5 months for those with del(11q22.3). But median PFS was more favorable in the group of subjects not having either of these chromosomal abnormalities.

In comparing PFS of patients with these two chromosomal abnormalities with PFS of patients without these chromosomal abnormalities, the authors concluded that each of these two chromosomal abnormalities is prognostic of poor outcome. The authors went a step further, by using these results to recommend that alternative treatments should be pursued for patients with del(17p13.1) or del(11q22.3). These alternative treatments include use of alemtuzumab, flavopiridol, and stem cell transplantation.

The following concerns semantics. In view of the heterogeneous nature of B cell CLL, this disease has been classed according to cytogenetics, for example whether the blasts have del(17p13.1) cyotogenetics or have del(11q22.3) cytogenetics. But sometimes del(17p13.1) and del(11q22.3) are called biomarkers. The question of whether a given deletion is used to define a given type of CLL, or is used to refer to a biomarker, may be a matter of personal preference.

[246] Dewald GW, Brockman SR, Paternoster SF, et al. Chromosome anomalies detected by interphase fluorescence in situ hybridization: correlation with significant biological features of B-cell chronic lymphocytic leukaemia. *Br J Haematol*. 2003;121:287–295.