VII. CYTOGENETICS AS A PROGNOSTIC MARKER – THE GREVER STUDY OF CLL

The chromosomal abnormalities in CLL include the following:

- del(13q14.3);
- trisomy 12;
- del(17p13.1); and
- del(11q22.3).

The term "del" means chromosomal deletion. Of these, deletions of 17p13.1 and 11q22.3 are associated with poorer prognosis, while the 13q14.3 deletion is associated with better prognosis (242).

The following concerns a clinical trial on CLL, where one of the goals was to determine if either of these two cytogenetic abnormalities, del(17p13.1) and del(11q22.3), might be correlated with poor survival, relative to survival patients whose cells did not contain these particular abnormalities.

Grever et al. (243) conducted a clinical trial of CLL, where study subjects (235 subjects total) were allocated to two arms. The two arms were:

- Arm A. Fludarabine alone
- Arm B. Fludarabine plus cyclophosphamide.

Treatment was for six cycles, each cycle lasting one month, and all study subjects were monitored for about 50 months. The results are shown in Table 17.5 and demonstrate that the combination of the two drugs worked better than fludarabine alone.

The following concerns the endpoint of complete response (CR). The Grever study used the endpoint of complete response, where the definition was provided by another publication by the same researchers (244). The definition appears in the footnote below (245).

Now let us turn from data that distinguish Arm A treatment from Arm B treatment, to data that correlate cytogenetic abnormalities with progression-free survival. This concerns methodology. The two types of chromosomal anomalies, del(17p13.1) and del(11q22.3), were determined by fluorescent probes. PBMCs were isolated at

[242] Woyach JA, Heerema NA, Zhao J, et al. Dic(17;18)(p11.2; p11.2) is a recurring abnormality in chronic lymphocytic leukaemia associated with aggressive disease. *Br J Haematol*. 2010;148:754–759.

[243] Grever MR, Lucas DM, Dewald GW, et al. Comprehensive assessment of genetic and molecular features predicting outcome in patients with chronic lymphocytic leukemia: results from the US Intergroup Phase III Trial E2997. *J Clin Oncol*. 2007;25:799–804.

[244] Blum KA, Young D, Broering S, et al. Computed tomography scans do not improve the predictive power of 1996 National Cancer Institute-Sponsored Working Group Chronic Lymphocytic Leukemia Response Criteria. *J Clin Oncol*. 2007;25:5624–5629.

[245] Complete response was the absence of lymphadenopathy and organomegaly by physical examination, absolute lymphocyte count (ALC) no higher than 5,000/μL, absolute neutrophil count (ANC) of at least 1,500/μL, platelets more than 100,000/μL, hemoglobin more than 11.0 g/dL, and bone marrow without lymphoid nodules and fewer than 30% lymphocytes.