

degree to which the amount BCR-ABL mRNA is reduced by therapy (198). When reporting the expression of BCR-ABL in the clinical context, the amount of mRNA is stated using an international scale. The medical community has accepted the BCR-ABL assay as a prognostic tool, as shown by the clinical trial of Saglio et al. (199) where BCR-ABL expression was used as the primary endpoint in a study of CML. This study compared the efficacy of nilotinib (BCR-ABL inhibitor) with imatinib, and found nilotinib to be superior in efficacy. Jabbour et al. (200) described the uses and limitations of the BCR-ABL assay as a prognostic tool.

e. Cytogenetics for diagnosis and prediction – CLL

In CLL, the most frequent aberrations are represented by 13q-, 11q-, + 12, 6q-, 17p- and 14q32/IGH translocations (201). Some of these forms of abnormal cytogenetics, as well as certain gene mutations, serve as prognostic markers in chronic lymphocytic leukemia. The 17p deletion (17p-), the 11q deletion (11q-), and the TP53 mutation indicate negative prognosis for CLL. Over 80% of CLL patients with the 17p deletion also carry a TP53 mutation. The 17p deletion and the TP53 can occur independently of each other, and both predict poor outcome (202). According to Badoux et al. (203) deletions of 17p or mutations of TP53 indicate a very poor prognosis, being predictive of short time for disease progression, lack of response to therapy, and short overall survival.

In a study of 268 CLL patients, TP53 mutations occur in 3.7% of patients (n = 10), where 7/10 cases showed a concomitant 17p deletion (204). Thus, there is a high prevalence of TP53 mutation in 17p-deleted patients. Only three (1.1%) of the newly diagnosed patients carried TP53 mutations without 17p deletion.

A totally separate study of CLL found TP53 mutations in 8.5% of patients (28 of 328 patients), where TP53 mutations in the absence of 17p deletions were found in

¹⁹⁸ Hughes T, Deininger M, Hochhaus A, et al. Monitoring CML patients responding to treatment with tyrosine kinase inhibitors: review and recommendations for harmonizing current methodology for detecting BCR-ABL transcripts and kinase domain mutations and for expressing results. *Blood*. 2006;108:28–37.

¹⁹⁹ Saglio G, Kim DW, Issaragrisil S, et al. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. *New Engl J Med*. 2010;362:2251–2259.

²⁰⁰ Jabbour E, Cortes JE, Kantarjian HM. Molecular monitoring in chronic myeloid leukemia: response to tyrosine kinase inhibitors and prognostic implications. *Cancer*. 2008;112:2112–2118.

²⁰¹ Cavazzini F, Ciccone M, Negrini M, Rigolin GM, Cuneo A. Clinicobiologic importance of cytogenetic lesions in chronic lymphocytic leukemia. *Expert Rev Hematol*. 2009;2:305–314.

²⁰² Stilgenbauer S, Zenz T. Understanding and managing ultra high-risk chronic lymphocytic leukemia. *Hematology Am Soc Hematol Educ Program*. 2010;481–488.

²⁰³ Badoux XC, Keating MJ, Wierda WG. What is the best frontline therapy for patients with CLL and 17p deletion? *Curr Hematol Malig Rep*. 2011;6:36–46.

²⁰⁴ Zainuddin N, Murray F, Kanduri M, et al. TP53 Mutations are infrequent in newly diagnosed chronic lymphocytic leukemia. *Leuk Res*. 2011;35:272–274.