In addition to t(9;22)(q34;q11) (Philadelphia chromosome), Brazma et al. (226) and Nacheva et al. (227) have identified a number of other chromosomal abnormalities in CML, where these abnormalities occur, for example, at 1p36, 5q21, 7p12, 8q24, 9p21, 9q34, 9q34, 14q11, 14q32, and 22q11. Moreover, a variety of gene mutations have been associated with CML, most notably, affecting *CDKN2A/2B*, *EVI-1*, *RB*, *MYC*, and *p53* genes (228). The possibility that these chromosomal abnormalities and genetic mutations contribute to the progression of CML, or can be used as a prognostic marker, is currently being explored. The following concerns the time point for conducting an analysis of chromosomal aberrations and gene mutations. Evidence suggests that the BCR/ABL1 fusion protein itself can induce the accumulation of additional genetic lesions, including point mutations, gene amplifications, genome loss and chromosome translocations, and that these mutations drive the malignant process (229).

e. Utility of Philadelphia Chromosome in Diagnosis, Drug Target, and for Assessing Response

Philadelphia chromosome, or its expressed mRNA and polypeptide, can be used as follows:

- Diagnosing leukemia;
- As a target of kinase inhibitors;
- To measure objective response to chemotherapy, for example, in the minimal residual disease (MRD) assay (230,231,232);
- In deciding to increase drug dose or to change to a second-line treatment (233).

Leukemias that are caused by a mutation called *Philadelphia chromosome* are CML and Philadelphia chromosome-positive ALL. The mutation is a translocation, identified as, t(9;22)(q34;q11). This abnormal chromosome contains a fusion gene, consisting of the *ABL* gene and the *BCR* gene, producing the *BCR-ABL* oncogene. This oncogene expresses an

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