ADDITIONAL CYTOGENETIC ABNORMALITIES ARE A POWERFUL MARKER FOR RESISTANCE AND DISEASE PROGRESSION IN CML.

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Detection of t(9;22)(q34;q11) translocation (Philadelphia chromosome), which results in the production of BCR-ABL-1 fusion protein, is a recognized cytogenetic hallmark for CML diagnosis. Introduction of tyrosine kinase inhibitors (TKIs) which specifically target ABL-1 have revolutionized treatment and outcome for patients with CML. TKI therapy, being administered for a long period of time, needs a strict protocol for patient monitoring in order to assess response and resistance to the treatment. Presence or absence of Ph-positive cells in the bone marrow serves as a powerful early indicator of response for CML patients during therapy. Additional cytogenetic changes detected at any moment during treatment, including additional abnormalities in the BCR–ABL1-negative cells, provide useful prognostic information for patient risk stratification.

In this study we evaluated cytogenetic response of patients with CML during TKI therapy.

Materials and Methods: In this study, we analyzed 428 samples from CML patients – 101 samples from patients at presentation and 327 follow-up samples. We analyzed bone marrow specimens using conventional cytogenetics.

Results: From 101 patient samples at presentation – 68 presented Ph chromosome without any additional cytogenetic abnormalities, 14 presented, besides Ph chromosome, additional cytogenetic abnormalities and 1 patient was negative for Ph chromosome on standard cytogenetic analysis but it was confirmed to be BCR-ABL-1 positive both by FISH and PCR analysis. In 18 cases no metaphases were obtained and presence of BCR-ABL-1 fusion gene was detected using FISH analysis. From 327 follow-up samples – 233 was from patients treated with Imatinib, 65 was obtained from patients treated with Nilotinib and 29 from patients with Dasatinib. From 233 patients treated with Imatinib for 39 samples no metaphases were obtained and samples were evaluated using FISH. In 20 cases additional cytogenetic aberrations were identified either in Ph+ or Ph- cells. In Nilotinib treatment group – for 9 samples no metaphases were obtained and 6 with additional cytogenetic findings. In Dasatinib treatment group – for 7 samples no metaphases were obtained and 3 with additional cytogenetic abnormality.

Conclusion: For presentation samples additional cytogenetic findings were strongly associated with accelerated phase of disease or blast crisis. For all treatment groups not only Ph+ cell identification but especially additional cytogenetic findings were a strong predictor of resistance to treatment and disease progression. In this study we show the power of cytogenetics to detect early markers of disease resistance and progression.