Determination of Imatinib in the Blood Cells of Chronic Myelogenous Leukemia Patients by Ion-Trap Mass Spectrometry

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Imatinib mesylate is a standard first-line therapy for patients with chronic myelogenous leukemia. However, there is still a significant proportion of these patients who reflect sub-optimal responses or fail imatinib therapy. Knowledge of the distribution within the studied system (e.g., peripheral blood) may be of high importance for understanding the principles of drug action and possible patient resistance to treatment. Intracellular, or more precisely cell-associated, imatinib concentrations in patients, were shown to be higher compared to those in plasma, but still only limited data related to the methodology aspects of cell-associated concentrations are available. Herein is presented an assessment of the cell-associated imatinib determination assay by mass spectrometry. Three approaches were evaluated to isolate cells from the peripheral blood of chronic myelogenous leukemia patients. Erythrocyte lysis was found to cause substantial leakage of cell-associated imatinib in the first step. Selected alternative procedures utilizing density gradients did not affect the cell-associated imatinib concentration significantly. Cell isolates were subjected to flow cytometry which revealed differences in the population composition of peripheral blood cell isolates among individual patients indicating that the cell isolate composition should be addressed with the cell-associated imatinib concentration. The proposed approach may be utilized for the determination of intracellular concentration of imatinib and for other drugs in which the intracellular concentration plays a key role in the therapy.