Monitoring of an anti-cancer drug concentration in human blood

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Chronic Myelogenous Leukemia (CML) is a form of cancer that increases number of white blood cells in the blood by uncontrolled proliferation of white blood cells in the bone marrow. Diagnosis of CML usually takes place in the initial chronic phase and if left untreated it progresses to an accelerated phase in three to five years. According to the statistics published by the U. S. National Cancer Institute, most of the CML patients are diagnosed in the latter part of their life with an average of 64 years of age; the incidence rate is about 1.6 per 100000/year in average.

Until the introduction of imatinib, interferon alfa was widely regarded as the best treatment for CML patients who cannot be treated with bone marrow transplantation in the chronic phase of CML. The interferon drug is known to cause a number of side effects, especially in older patients. The bone marrow transplantation can only be applied to a limited number of patients and it may cause serious complications or even death. Imatinib, commercially available as Gleevec® or Glivec®, is therefore regarded as the first cancer treatment that selectively eliminates cancer cells rather than destroying all the rapidly dividing cells. It was first clinically tried for treating CML patients in 1998 and received approval of U.S. Food and Drug Administration in 2001.

Imatinib is taken orally and its concentration in blood has to be within a certain range in order to achieve an optimal clinical response. Nausea, changes in blood counts, fluid retention, muscle cramps are some of the side-effects that imatinib treated CML patients experience, which are however considered manageable and much less severe than that of the interferon therapy. Imatinib concentration in cancer patients treated within the recommended dosage does vary depending on several factors like individuals' drug metabolism.

Recent findings have suggested that monitoring imatinib concentration in CML patients is useful for understanding of treatment failures, suboptimal response of patients receiving recommended dosage. To determine imatinib concentration in CML patients' blood, two methods have been developed based on liquid chromatography (LC) and direct analysis in real time (DART) mass spectrometry (MS). The LC method is capable of quantifying very low and a wide range of imatinib concentrations in human blood. The method developed based on DART is of its first kind for imatinib quantification and suitable for a quick estimation of imatinib concentration.

Plasma samples containing known amounts of imatinib received from a reference laboratory in Bordeaux, France were analysed by the developed methods. The results were satisfactory and no significant deviation was seen compared to the provided reference values. The imatinib concentrations in plasma samples of 10 CML patients were determined by means of the LC-MS method. The measured imatinib concentrations varied over a wide range where 8 patients exceed the clinically recommended imatinib concentration in human blood.

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