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P90. PLASMA CONCENTRATIONS OF IMATINIB AND N-DESMETHYL IMATINIB IN CHRONIC MYELOID LEUKEMIA PATIENTS

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Chronic myeloid leukemia (CML) is a serious myeloproliferative cancer. Imatinib is the first line treatment. Imatinib's primary metabolism depends on the presence of cytocrome P450 (CYP450) enzymes. The active metabolite is N-desmethyl imatinib (norimatinib). Pharmacologic effects of imatinib and norimatinib are similar. Norimatinib can accumulate in the plasma 10-30% of imatinib. The aim of this study was to analyze certain parameters which maintain their importance in clarifying imatinib's pharmacologic effects.

To investigate plasma concentrations, 41 CML patients (18 women, 23 men) on 400 mg oral imatinib treatment at Ankara University School of Medicine Hematology Department in Turkey were included. Mean age and mean treatment period were 46.97 and 4.29 years, respectively.

Pharmacokinetic analysis of imatinib and norimatinib was performed by liquid chromatograhy tandem mass spectometry (LC-MS/MS). LOQ values for imatinib and norimatinib were 66 ppb and 62.5 ppb, respectively, whereas LOD values were 30 ppb and 25 ppb, respectively. Recovery of imatinib and norimatinib were recorded as 98.45% and 92.47%, respectively.

Average plasma imatinib-norimatinib levels were 4 ppm and 1 ppm, respectively. Sigmoidal 2-tailed Pearson correlation test revealed significant correlation between concentrations of the two compounds. However, individual norimatinib/imatinib percentages suggested intraidividual variability to drug response (min. value 7.917%, max. value 58.72%).

Statistical results are in line with scientific knowledge already established for imatinib and its pharmacokinetics. Nevertheless, individual results have shown that pharmacologic effects of imatinib may differentiate among patients. Further studies related to individual characteristics and environmental factors are necessary to enlighten intraindividual differences of imatinib behavior.