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sarcoma

1429P THERAPEUTIC DRUG MONITORING OF IMATINIB IN GIST PATIENTS

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Aim: Imatinib is a drug of choice for the treatment of gastrointestinal stromal tumors (GIST), and some studies suggest that a minimum plasma concentration (Cmin) of 1 mg/L should be obtained to ensure the achievement of maximum therapeutic benefit from the drug. However, the pharmacokinetics of imatinib is widely variable among patients and a therapeutic drug monitoring (TDM) should be adopted. Therefore, the rationale of the study was to evaluate the feasibility of a TDM protocol in GIST patients and any possible correlation with treatment efficacy and/or toxicity.

Methods: Twelve GIST patients, 6 men and 6 women (median age and range, 65.9 and 49-71.7 years and 65.3 and 52.8-80.4 years, respectively), receiving imatinib at the daily median dose of 400 mg (range, 200-800 mg/day), were enrolled. Blood samples were obtained during follow-up visits at any time after drug intake and the time elapsed between imatinib administration and blood withdrawal was carefully recorded. Plasma concentrations of imatinib were measured by a commercially-available kit (Chromsystems, Munich, Germany), then Cmin values were predicted adopting a noncompartmental pharmacokinetic analysis. Finally, clinical data regarding response and tolerability were recorded.

Results: Cmin values were higher in women (mean±SD, 1.730±0.867 mg/L) than in men (0.975±0.584 mg/L, p=0.111), and there was a linear correlation (r=0.641, p<0.05) among predicted Cmin values and imatinib daily dose. No significant correlations were observed between Cmin values and treatment effectiveness. Conversely, it is interesting to note that 4 patients (3 women and a man) suffered from grade 2 CTC-NCI toxicity (peripheral oedema, anemia, asthenia and diarrhea) and 3 of them had predicted highest Cmin values (range, 2.04-2.84 mg/L). Statistical analysis suggested a trend for a possible association between drug-induced toxicity and Cmin values higher than 2 mg/L (chi-square test, p=0.067).

Conclusions: Although imatinib is characterized by a good tolerability and a linear relationship between daily dose and plasma concentrations, an interindividual varability in drug disposition exists and occurrence of toxicities may be associated with the highest Cmin values, hence strenghtening the role of TDM protocols in GIST patients receiving imatinib.

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