Titel des Beitrags:
Pharmacokinetic and Clinical Phase II Trial of Imatinib in Patients with Impaired Liver Function and Advanced Hepatocellular Carcinoma

Abstract:
Objectives: No effective chemotherapy for advanced hepatocellular carcinoma (HCC) exists. Expression of the platelet-derived growth factor receptor (PDGFR) has been demonstrated in HCC, which may derive from hepatic stem cells that express c-kit. The aim of this trial was to evaluate imatinib, a tyrosine kinase inhibitor of PDGFR and c-kit, in patients with advanced HCC and impaired liver function. Patients and Methods: Patients were treated with 400–600 mg imatinib daily. Immunohistochemical staining was performed for PDGFR and c-kit. Response was assessed by CT scans every 8 weeks. For pharmacokinetics studies, 74 plasma samples were assessed. Results: Of the 17 patients enrolled in the study, 15 were evaluable for response. Only 1 tumor was positive for PDGFR and none was positive for c-kit. Grade 3/4 neutropenia occurred in 2 patients (1 had neutropenic fever). There was no objective response, and 5 (33%) patients had stable disease. Median time to treatment failure was 1.8 months in the whole study cohort and 3.7 months in the patients with stable disease. Patients treated with 400 mg imatinib did not significantly differ in pharmacokinetics from patients with chronic myelogenous leukemia (CML). Conclusion: In this small group of patients with advanced, mostly PDGFR- and c-kit-negative HCC, imatinib showed no therapeutic effect. In contrast to CML patients,
the pharmacokinetics of imatinib were not significantly affected by impaired liver function.

**Stichworte:**
c-kit; Hepatocellular carcinoma; Imatinib; Phase II clinical trials; Platelet-derived growth factor receptor

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