Individual Fluorouracil Dose Adjustment in FOLFOX Based on Pharmacokinetic Follow-Up Compared With Conventional Body-Area-Surface Dosing: A Phase II, Proof-of-Concept Study

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Drug Monitoring [7], Efficacy [8], Fluorouracil [9], Personalized medicine [10], toxicity [11]
Background To compare the efficacy and safety of pharmacokinetically (PK) guided fluorouracil (5-FU) dose adjustment vs. standard body-surface-area (BSA) dosing in a FOLFOX (folinic acid, fluorouracil, oxaliplatin) regimen in metastatic colorectal cancer (mCRC). Patients And Methods A total of 118 patients with mCRC were administered individually determined PK-adjusted 5-FU in first-line FOLFOX chemotherapy. The comparison arm consisted of 39 patients, and these patients were also treated with FOLFOX with 5-FU by BSA. For the PK-adjusted arm 5-FU was monitored during infusion, and the dose for the next cycle was based on a dose-adjustment chart to achieve a therapeutic area under curve range (5-FUODPM Protocol). Results The objective response rate was 69.7% in the PK-adjusted arm, and median overall survival and median progression-free survival were 28 and 16 months, respectively. In the traditional patients who received BSA dosage, objective response rate was 46%, and overall survival and progression-free survival were 22 and 10 months, respectively. Grade 3/4 toxicity was 1.7% for diarrhea, 0.8% for mucositis, and 18% for neutropenia in the dose-monitored group; they were 12%, 15%, and 25%, respectively, in the BSA group. Conclusions Efficacy and tolerability of PK-adjusted FOLFOX dosing was much higher than traditional BSA dosing in agreement with previous reports for 5-FU monotherapy PK-adjusted dosing. Analysis of these results suggests that PK-guided 5-FU therapy offers added value to combination therapy for mCRC.

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