UFT/LV in heavily pretreated patients

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Anti-Cancer Drugs 2003, **14 (suppl 2)**:S8

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Fluorouracil in conjunction with leucovorin ± irinotecan or oxaliplatin is considered as the mainstay first-line treatment in many patients with metastatic colorectal cancer. In patients with disease progression following first-line therapy with single agent fluorouracil plus leucovorin, subsequent combination chemotherapy regimen may include oxaliplatin and irinotecan. The case study below describes the use of oral tegafur-uracil/leucovorin (UFT/LV) in a heavily pre-treated patient.

A 50-year old female had an anterior rectal resection in December 1999 due to a large tubulovillous adenoma with severe dysplasia, but with no evidence of invasive growth. In January 2001, the patient was diagnosed with an isolated liver metastasis and had a hemihepatectomy. Histology revealed mucinous adenocarcinoma corresponding to a typical metastasis of colorectal cancer. In August 2001, a CT scan showed lung nodules (<1 cm) and liver metastases (≤4 cm). The patient was recruited in a European Organisation for Research and Treatment of Cancer (EORTC) study and randomised to receive intravenous (IV) fluorouracil (2600 mg/m^2 over 24 h) and leucovorin (500 mg/m^2) every 6 weeks. After one cycle, the hepatic lesions had progressed and the pulmonary metastases were stable. Further treatment comprised single agent irinotecan 350 mg/m^2 every 3 weeks and after 4 treatment cycles the disease was stable, but was found to be progressive after 6 cycles. In March 2002, third-line chemotherapy was started with capectabine 1000 mg/m^2 for days 1–14 plus oxaliplatin 130 mg/m^2 on day 1 repeated every 3 weeks. Evaluation of response after two cycles found the disease was stable and after 4 cycles there were signs of progressive disease with 100% increase in lung metastases. The patient wanted to continue with therapy and fourth-line chemotherapy was initiated with UFT 300 mg/m^2/day plus leucovorin 90 mg/day for 28 days, every 35 days. The disease was stable after the first and second cycles; the third cycle is ongoing. To date, there have been no severe toxicities with no evidence of diarrhoea, stomatitis and hand-foot syndrome. Haematological toxicities have been mild.

For optimal palliation in metastatic disease, patients require treatment to improve efficacy but with minimal toxicity. Despite previous chemotherapy with several single or combination anti-cancer drugs, our patient requested further treatment and had stable disease without severe toxicity with UFT/LV. Future clinical trials of UFT/LV in refractory colorectal cancer should assess its effect on quality of life and amelioration of disease-related symptoms which correspond more closely with palliative benefit in this clinical setting.