Combination of UFT/LV with radiotherapy

W. Wagner

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Paracelsus Klinik, 49076 Osnabrück, Germany.

Success with fluorouracil as a radiosensitizer [1] has led us to explore the feasibility of concurrent oral tegafur-uracil/leucovorin (UFT/LV) with radiation therapy in an attempt to improve symptom control in a small group of patients with recurrent rectal cancer.

Nine patients (five males and four females, median age of 68 years [range, 55–72]) with Duke's stage B2 + C rectal cancer had been pretreated according to the GI Ontario National Cancer Institute guidelines of fluorouracil 450–500 mg/m^2 intravenous (IV) bolus combined with radiotherapy at 1.8 Gy, 5 doses per week (total 50.4 Gy). After diagnosis of recurrent disease, radiochemotherapy was initiated and comprised another course of 30 Gy irradiation given as 1.2 Gy fractions over 25 days targeted at the gross tumour and UFT 200 mg/m^2/day plus oral LV 90 mg/day for 25 days. There were no grade 3 or 4 toxicities. Grade 1 or 2 diarrhoea was experienced by five patients, grade 1 neutropenia by one patient, and grade 1/2 nausea/emesis by two patients. All patients had some pain control, with five experiencing complete pain relief and four experiencing pain reduction. A matched pair analysis of our group with historical controls who had received radiotherapy alone or radiotherapy plus fluorouracil was undertaken. The controls were almost identical for tumour localisation, volume and pain. Of those treated with radiotherapy alone, six patients had some pain control and three had no pain reduction, while of those treated with fluorouracil and radiotherapy, eight patients had some pain control and one had no pain reduction.

The combination of radiotherapy and chemotherapy in patients with rectal carcinoma may improve local control but at the risk of increased toxicity. Our experience suggests that UFT/LV and radiation therapy is a feasible combination that is well-accepted and offers pain control.

Studies have reported use of combined modality treatment with UFT/LV and radiotherapy for rectal cancer. A dose-escalation study was undertaken to evaluate the safety of UFT plus LV in combination with pelvic radiation in patients with recurrent rectal cancer. Nineteen patients received radiation to the pelvis up to a total of 50.4 Gy, at 1.8 Gy/day fractions 5 days per week for 5 weeks followed by a boost of 5.4 or 9.0 Gy to the gross tumour volume. The maximum tolerated dose (MTD) of UFT was 400 mg/m^2/day due to the occurrence of dose-limiting diarrhoea and emesis. Doses of UFT 350 mg/m^2/day plus LV 90 mg were recommended for further chemoradiation trials [2].

A recent study assessed the impact of pre-operative radiation combined with UFT plus LV on tumour response and sphincter preservation in 41 patients with resectable rectal carcinoma [3]. Chemotherapy comprised UFT 300 or 350 mg/m^2 on days 1 to 14, repeated every 28 days and LV (IV dosing on day 1 and oral dosing on days 2–14). Six additional cycles were given post-surgery. Tumour downstaging was observed in 35 patients (61%; 95% confidence interval [CI]: 45% to 76%) and the incidence of sphincter-saving surgery was increased from 39% at diagnosis to 63% after pre-operative treatment. The use of UFT plus LV is under investigation as an adjunct to pre-operative radiotherapy in a phase I/II study [4]. Sixteen patients with T2-4 N0-1 M0 rectal adenocarcinoma took part in the dose escalation phase of the study where a fixed dose of radiation (45 Gy at 180 Gy/day over 5 weeks) was combined with escalating doses of UFT plus a fixed dose of 30 mg/day oral LV given over 28 days concomitant with the first 4 weeks of radiotherapy. Grade 4 gastrointestinal toxicity occurred in two patients. The MTD of UFT was defined as 240 mg/m^2/day and a further 20 patients are to be enrolled in the second phase of the study for assessment of response with this dose.

References

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