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GASTROINTESTINAL CANCER

Introducing new steps with a FOxTROT

In certain cancers related to the digestive system—such as oesophageal, gastric and rectal cancer—preoperative chemotherapy is more effective than any similar regimen given postoperatively. Because postoperative chemotherapy is habitually given at least 3 months after diagnosis, treatment before surgery may be more effective at eradicating early-stage metastatic disease. Moreover, shrinking tumours before surgery not only facilitates removal of all the tumour by the surgeon, but also might reduce tumour cell spreading during the procedure.

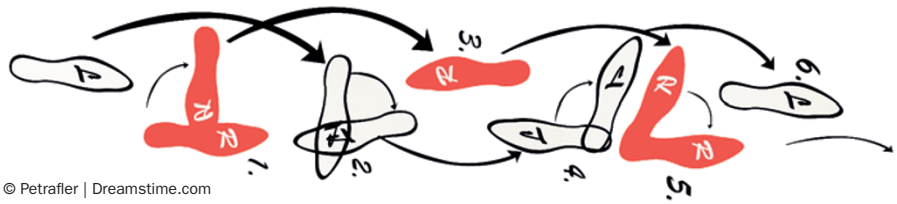
Despite all these potential benefits, postoperative chemotherapy is regarded as the standard of care for patients with colon cancer to avoid tumour growth during the preoperative treatment (which could result in bowel obstruction and subsequent high morbidity emergency surgery) and to avoid inaccurate preoperative tumour staging, which may result in inadequate use of chemotherapy for low-risk patients.

On the basis of the successful use of preoperative chemotherapy in related cancers, the Surgical Trials Committee of the UK's National Cancer Research Institute Colorectal Cancer Clinical Studies Group (made up of surgical, oncological and statistical experts) are assessing preoperative chemotherapy for locally advanced colon cancer in a multicentre study. "FOxTROT (Fluoropyrimidine Oxaliplatin and Targeted Receptor Pre-Operative Therapy) is a randomized clinical trial designed to assess whether 6 weeks of an effective combination chemotherapy regimen given preoperatively to patients with radiologically staged, locally advanced, but potentially resectable colon cancer improves cure rates compared with standard postoperative chemotherapy", explains Richard Gray, on behalf of the FOxTROT collaborative group. The primary end points of the pilot phase of the study were feasibility, safety, and tolerance of preoperative therapy, as well as the accuracy of radiological staging and downstaging of the resected tumour. Moreover, the trial also assessed whether patients with *KRAS* wild-type tumours would also benefit from receiving panitumumab, an anti-EGFR antibody, during the first 6 weeks of the preoperative therapy.

The pilot study enrolled 150 patients from 35 centres who were randomly assigned to receive either preoperative and postoperative oxaliplatin-based chemotherapy ($n = 99$) or postoperative chemotherapy alone ($n = 51$). "We found that 6 weeks of preoperative 'OxMdG' chemotherapy are feasible and produce significant downstaging of the tumours with acceptable toxicity and perioperative morbidity," explains Dion Morton, the surgeon leader of the study.

Does this mean that the current standard practice for high-risk colon cancer will change? Gray admits that, although these results are highly promising, a larger randomized trial is needed "the full FOxTROT study is underway aiming to randomize over 1,000 patients. If preoperative therapy results in fewer recurrences, as well as tumour downstaging, the established pathway of surgery then chemotherapy in the management of colon cancer could potentially change."

M. Teresa Villanueva



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