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GASTROINTESTINAL CANCER

New drug shows promise in refractory colorectal cancer

Treatment of colorectal cancer has improved, but for patients with tumours that are refractory to standard cytotoxics or novel targeted therapies, such as bevacizumab and cetuximab, there is no current standard-of-care and therapy options are extremely limited. There are a number of drugs in development for the treatment of these patients, and now one of them has shown considerable promise in a phase II, randomized trial.

The present clinical trial was based on results obtained from a phase I trial that assessed the novel oral nucleoside antitumour agent, TAS-102, in patients with solid tumours. In this first trial, 18 of the 21 patients had metastatic colorectal cancer, and in these patients a benefit in overall survival, disease control rate and progression-free survival was observed. This benefit was better than observed when treating patients who were refractory to cytotoxics with the targeted therapies panitumumab and cetuximab. The lead author of the phase II study,

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Takayuki Yoshino, explains: “these results suggested that TAS-102 could further improve the outcomes of patients with unresectable metastatic colorectal cancer who have already received conventional chemotherapies with a fluoropyrimidine, irinotecan, and oxaliplatin.”

The phase II trial randomly assigned 169 patients with heavily pretreated metastatic colorectal cancer to either TAS-102 or placebo, in addition to best supportive care, and patients were followed up for a median of 11.3 months. Yoshino elaborates, “patients who were enrolled in the study have no other treatment choice and [the trial] was being implemented with the aim of prolonging life by treating with this drug. Therefore, we thought that the primary end point should be overall survival.”

Encouragingly, in these patients, the overall survival was significantly improved in the patients receiving TAS-102 compared with those receiving best supportive care only (9.0 months versus 6.6 months). It is clear that the drug is associated with some adverse effects, but these seem to be manageable; serious adverse effects were seen in 21% of patients receiving TAS-102, compared with 9% in the placebo group.

“We are conducting an international phase III trial to confirm the clinical benefits of TAS-102 in all populations,” says Yoshino, and it is clear that we will need to wait for the results of this trial before practice can change. At this stage, perhaps we can be cautiously optimistic.

Rebecca Kirk

Original article Yoshino, T. *et al*. TAS-102 monotherapy for pretreated metastatic colorectal cancer: a double-blind, randomised, placebo-controlled phase 2 trial. *Lancet Oncol*. doi:10.1016/S1470-2045(12)70345-5