

GASTROINTESTINAL CANCER

FOLFIRI plus cetuximab—preferred first-line treatment for mCRC

First-line treatment for metastatic colorectal cancer (mCRC) is regarded as the most-important phase of therapy because not all patients receive subsequent therapy, and the effect on patient outcome, in the first-line setting, is often greater. No trial has investigated whether the 5-fluorouracil-based regimen FOLFIRI combined with the EGFR-targeting agent cetuximab is better than FOLFIRI combined with the anti-VEGF agent bevacizumab. This situation prompted researchers to conduct the FIRE-3 trial—a head-to-head, open label, randomized phase III study to compare FOLFIRI and cetuximab with FOLFIRI and bevacizumab in patients with stage IV mCRC with wild-type *KRAS* tumours.

The primary end point of the trial was objective response and secondary end points included progression-free survival (PFS) and overall survival. The objective response rates (complete or partial) between the two treatment arms were similar, as was the median PFS. However, overall survival was significantly longer

in patients receiving the cetuximab–FOLFIRI combination compared with bevacizumab and FOLFIRI (28.7 months versus 25.0 months, $P=0.017$). Adverse effects in both arms were similar. The survival advantage was more pronounced in patients wild-type for all *KRAS* exons compared with patients with *KRAS* wild-type within exon 2 only; by contrast, patients with *KRAS* mutations not in exon 2 derived a greater benefit from bevacizumab plus FOLFIRI.

The authors of the study point out that, as this was an open-label study, some bias might exist; nevertheless, overall, the data indicate cetuximab as the preferred front-line agent when combined with FOLFIRI.

Lisa Hutchinson

Original article Heinemann, V. *et al.* FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial. *Lancet Oncol.* doi:10.1016/S1470-2045(14)70330-4