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GASTROINTESTINAL CANCER

BEVACIZUMAB: HOPE AFTER PROGRESSION

The results of a phase III randomized study have shown that patients with metastatic colorectal cancer whose tumours have progressed after first-line chemotherapy and anti-VEGF therapy with bevacizumab might benefit from continued anti-VEGF therapy in the second line.

"We hypothesized that, because of the complementary modes of action of anti-VEGF and chemotherapeutic agents, bevacizumab could continue to benefit patients even after resistance to chemotherapy has developed," explains lead investigator Stefan Kubicka. The multicentre trial of >800 patients randomly assigned participants to bevacizumab plus chemotherapy or chemotherapy alone. The chemotherapy regimen assigned depended on what the individual patient had received in the first line. For example, a patient who had previously received (and progressed on) oxaliplatin-based therapy was given irinotecan-based therapy and vice versa. All patients had already received ≥3 months of bevacizumab before being enrolled.

The median overall survival was 11.2 months for patients who received bevacizumab and 9.8 months in the chemotherapy-alone group, a statistically significant difference. Progression-free survival was also prolonged for those receiving bevacizumab, which was "generally very well tolerated, with no unexpected adverse events arising from the combination with chemotherapy or the long duration of treatment," explains Kubicka.

Although the hypothesis that maintaining inhibition of angiogenesis across multiple lines of chemotherapy might be beneficial has been proposed before, and supported by cohort studies, this is the first randomized trial to show the extent of this benefit. "This principle might also be relevant in other VEGF-dependent tumours," says Kubicka. The approach is currently under investigation in metastatic breast and non-small-cell lung cancers.

As anti-VEGF therapy becomes increasingly prevalent, these data indicate that patients can tolerate multiple challenges with bevacizumab. "In addition, we will hopefully find molecular markers to identify patients with metastatic colorectal cancer who will need therapies with broadly acting antiangiogenic agents," concludes Kubicka.

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Original article Bennouna, J. *et al.* Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): a randomised phase 3 trial. *Lancet Oncol.* doi:10.1016/S1470-2045(12)70477-1