

## GASTROINTESTINAL CANCER A PROMISING HORIZON FOR CEDIRANIB?

Overall survival for most patients with metastatic colorectal cancer (mCRC) is less than 2 years, hence effective treatment against this disease is needed. FOLFOX—an oxaliplatin-based chemotherapy regimen that comprises fluorouracil, leucovorin, and oxaliplatin—is frequently used as first-line treatment for mCRC. Combining FOLFOX with the VEGF-A antibody bevacizumab has prolonged progression-free survival (PFS), but not overall survival. Could cediranib, a tyrosine kinase inhibitor (TKI) that targets all three VEGF receptors, supersede bevacizumab in mCRC? Two new papers published in the same issue of *Journal of Clinical Oncology* address this question.

Hans-Joaquim Schmolli, leader of one of the studies, explains the different goals of these trials: “in phase I–II trials, it has been seen that cediranib is active in mCRC as single agent. This result was also seen in combination with chemotherapy and, thus, a phase III strategy was developed with two trials—Horizon II, which compares FOLFOX with and without cediranib, and Horizon III, which compares the FOLFOX bevacizumab regimen with FOLFOX plus cediranib.”

Horizon II, led by Paulo M. Hoff, enrolled 860 patients who received FOLFOX in combination with cediranib ( $n = 502$ ) or placebo ( $n = 358$ ). Although the addition of cediranib prolonged PFS (8.6 months versus 8.3 months), it had no significant effect on overall survival (19.7 months compared with 18.9 months). No significant differences in the secondary end points of objective response rate or duration of response could be detected either.

In Horizon III, patients received FOLFOX in combination with cediranib ( $n = 709$ ) or bevacizumab ( $n = 713$ ). There was no significant difference in PFS (9.9 months versus 10.3 months) or overall survival (22.8 months versus 21.3 months).

However, Schmolli is positive: “the clinical outcome in terms of PFS was absolutely equivalent to the standard FOLFOX–bevacizumab, proving that TKIs are as effective as bevacizumab. Therefore, this study might support further clinical research with this type of VEGF inhibitor in CRC.”

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**Original articles** Hoff, P.M. *et al.* Cediranib plus FOLFOX/CAPOX versus placebo plus FOLFOX/CAPOX in patients with previously untreated metastatic colorectal cancer: a randomized, double-blind, phase III study (HORIZON II). *J. Clin. Oncol.* doi:10.1200/JCO.2012.42.6031 | Schmolli, H.-J. *et al.* Cediranib with mFOLFOX6 versus bevacizumab with mFOLFOX6 as first-line treatment for patients with advanced colorectal cancer: a double-blind, randomized phase III study (HORIZON III). *J. Clin. Oncol.* doi:10.1200/JCO.2012.42.5355