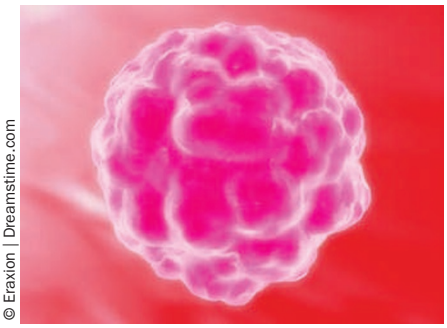
TARGETED THERAPIES

Panitumumab improves PFS in mCRC with wild-type *KRAS*



Colorectal cancer (CRC) is the third most common cancer in the USA, and more than 500,000 people die from CRC each year worldwide. Panitumumab, a fully human monoclonal antibody that targets EGFR, is an approved therapy for metastatic CRC. Mutated *KRAS* is a negative predictor of response to panitumumab, but wild-type *KRAS* is a positive predictor of response. Two phase III randomized trials were conducted to test the efficacy of panitumumab with fluorouracil, leucovorin and oxaliplatin (FOLFOX4) or fluorouracil, leucovorin and irinotecan (FOLFIRI) in the first-line and second-line settings, respectively.

Both trials showed that the addition of panitumumab to chemotherapy significantly improved progression-free survival (PFS) but only in patients with wild-type *KRAS*. In the PRIME trial, 1,183 patients were randomly assigned to panitumumab and FOLFOX4 or FOLFOX4 alone. In patients with wild-type *KRAS* (60%), the median PFS was 1.6 months longer than those receiving the combination. However, patients with mutated *KRAS* had a significantly worse PFS when treated with panitumumab. A nonsignificant trend for an overall survival advantage was also observed for wild-type *KRAS* patients receiving panitumumab.

In the second trial, 1,186 patients with metastatic CRC who had received one prior chemotherapy regimen were randomly assigned to panitumumab and FOLFIRI or FOLFIRI alone. 55% of patients had wild-type *KRAS* and in these patients a 2-month improvement in PFS for the combination arm was noted (5.9 months versus 3.9 months). In patients with mutant *KRAS*, there was no significant difference in PFS between the two arms. The objective response rate was also significantly improved in patients with wild-type *KRAS* who received panitumumab. In both trials, the adverse effects were comparable across arms and the incidence of skin toxicity and other adverse effects were as expected for this drug class.

"This trial confirms the importance of *KRAS* as a predictive biomarker of efficacy…in mutant *KRAS* patients, the addition of panitumumab resulted in a significant detrimental effect on PFS," comments Jean-Yves Douillard, lead investigator of the PRIME trial. "Panitumumab and FOLFIRI provides a convenient administration schedule with a manageable toxicity profile, representing an important new treatment option in patients with wild-type *KRAS* tumors", conclude the FOLFIRI trial researchers.

Lisa Hutchinson

Original articles Douillard, J.-Y. *et al*. Randomized phase III study of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: The PRIME study. *J. Clin. Oncol*. **28**, 4697–4705 (2010) | Peeters, M. *et al*. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. *J. Clin. Oncol*. **28**, 4706–4713 (2010)