

panitumumab adjunctive therapy

NEW INDICATIONS

No place in either first- or second-line treatment of metastatic colorectal cancer

● Adding *panitumumab* to standard protocols does not prolong survival but provokes additional adverse effects.



NOT ACCEPTABLE

The standard treatment for metastatic colorectal cancer is fluorouracil, alone or in combination with another cytotoxic drug, depending on the situation (Folfox or Folfiri protocol) (1).

Panitumumab monotherapy has an unfavorable harm-benefit balance in patients in whom the Folfox and Folfiri protocols have failed (2). *Panitumumab* (Vectibix[®], Amgen) is now authorised for first-line use in combination with the Folfox protocol, and for second-line use in combination with the Folfiri protocol, in patients whose tumours express the KRAS gene. Does the addition of *panitumumab* to these protocols prolong overall survival, and what are its adverse effects?

No increase in overall survival. Assessment of first-line *panitumumab* combination therapy is based on a randomised, unblinded trial comparing *panitumumab* + Folfox versus Folfox alone in 656 patients whose tumour cells expressed wild-type KRAS (3,4). Median overall survival was about 22 months in both groups, with no statistically significant difference between the groups (3). Median progression-free survival (primary endpoint) was about 6 weeks longer in the *panitumumab* group (9.6 versus 8 months; $p = 0.023$) (3).

Assessment of second-line *panitumumab* combination therapy is based on a randomised, unblinded trial comparing

panitumumab + Folfiri versus Folfiri alone in 597 patients whose tumours expressed wild-type KRAS (3,5). Median overall survival (a co-primary endpoint) was about 15 months, with no significant difference between the groups (3). Addition of *panitumumab* prolonged progression-free survival by about 2 months (5.9 versus 3.9 months, $p = 0.004$) (3).

A more burdensome adverse effect profile. Nearly all patients treated with *panitumumab* experience adverse effects, which include cutaneous, gastrointestinal and ocular disorders, interstitial pneumonia, pulmonary embolism, hypersensitivity reactions, nail dystrophy, and electrolyte disturbances. These disorders are often severe and sometimes life-threatening (2).

Worse yet, when combined with the Folfox or Folfiri protocol, *panitumumab* provokes significant additional adverse effects (3). New adverse effects were reported, including palmoplantar erythrodysesthesia, anorexia and weight loss (3).

Cases of cutaneous necrosis complicated by sepsis or life-threatening necrotising fasciitis have also been reported (6).

In practice. There is no evidence that *panitumumab* prolongs overall survival in patients with metastatic colorectal cancer, while it provokes additional, frequent and potentially life-threatening adverse effects. It is better to avoid using *panitumumab* altogether and to stick with standard protocols.

©Prescrire

panitumumab

Solution to be diluted for IV infusion

VECTIBIX[®]

- 100 mg or 400 mg of *panitumumab* (20 mg/ml) per vial

monoclonal antibody targeting EGFR

■ **New indications:** "(...)wild-type KRAS metastatic colorectal cancer (...)

- in first-line in combination with Folfox
- in second-line in combination with Folfiri".

[EU marketing authorisation, centralised procedure]

.....

Selected references from Prescrire's literature search.



In response to our request for information, Amgen provided us with published data only.

- 1- Prescrire Editorial Staff "Chemotherapy of metastatic colorectal cancer. Fluorouracil (+ folinic acid), oxaliplatin, irinotecan, combinations depending on the situation" *Prescrire Int* 2010; **19** (109): 219-224.
- 2- Prescrire Editorial Staff "Panitumumab. Metastatic colorectal cancer: don't make things worse!" *Prescrire Int* 2009; **18** (102): 157.
- 3- EMA - CHMP "Assessment report for Vectibix. EMEA/H/C/741/II/17" 17 March 2011: 69 pages.
- 4- Douillard JY et al. "Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (Folfox4) versus Folfox4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer" *J Clin Oncol* 2010; **28** (31): 4697-4705.
- 5- 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* 2010; **28** (31): 4706-4713.
- 6- Amgen "Lettre aux professionnels de santé sur l'association du panitumumab (Vectibix[®]) avec des complications infectieuses de réactions dermatologiques sévères, engageant le pronostic vital ou d'issue fatale, dont des cas de fasciite nécrosante" July 2012: 2 pages.