

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.