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.

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 Folfiri 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 Folfiri or Folfirinox protocol, *panitumumab* provokes significant additional adverse effects (3). New adverse effects were reported, including palmar-plantar erythrodysoesthesia, 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.

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**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 Folfirinox
  - in second-line in combination with Folfirinox

**[EU marketing authorisation, centralised procedure]**

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**Selected references from Prescrire’s literature search**

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


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): 4706-4705.

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 fascite nécrosante” July 2012: 2 pages.