panitumumab adjunctive therapy

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 (Folfiri or Folfox protocol) (1). Panitumumab monotherapy has an unfavorable harm-benefit balance in patients in whom the Folfox and Fol菲尔 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 Fol菲尔 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 + Fol菲尔 versus Fol菲尔 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 months versus 8 months; \( p = 0.023 \)) (3).

Assessment of second-line panitumumab combination therapy is based on a randomised, unblinded trial comparing panitumumab + Fol菲尔 versus Fol菲尔 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 months 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 Fol菲尔 or Fol菲尔 protocol, panitumumab provokes significant additional adverse effects (3). New adverse effects were reported, including palmoplantar erythrodysaesthesia, anorexia and weight loss (3).

Cases of cutaneous necrosis complicated by sepsis or life-threatening necrotizing 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.

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 Folifox – in second-line in combination with Fol菲尔" [EU marketing authorisation, centralised procedure]

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Selected references from Prescrire’s literature search

4- Douillard JY et al. “Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (Folfield) versus Folffield 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 (Fol菲尔) compared with Fol菲尔 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, engaçant le pronostic vital ou d’issue fatale, dont des cas de fasciite nécrosante” July 2012: 2 pages.