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 (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 + Folfiri 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. Newly 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 Folfiri protocol, panitumumab provokes significant additional adverse effects (3). New adverse effects were reported, including palmarplantar 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.

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]