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New Drug Mechanisms

In this series we draw attention to recently licensed medicines with an entirely new mechanism of action.

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Panitumumab

Indication

Panitumumab is indicated for the treatment of patients with metastatic colorectal cancer after failure of other cytotoxic drugs. Panitumumab is the first fully human monoclonal antibody directed against the epidermal growth factor receptor (EGFR). Cetuximab a half-human, half-murine antibody is also known for its EGFR blocking effects. Erlotinib is another tumour-suppressing drug that acts at the tyrosine kinase of the EGFR and preventing autophosphorylation (Figure). The EGFR plays an important role in all kinds of tumours and is one of the most important targets for growth-promoting hormones.

Mechanism

Panitumumab occupies the EGFR, thereby preventing binding of the endogenous ligands epidermal growth factor (EGF) or transforming growth factor-alpha. Panitumumab is a pure antagonist and induces internalization of EGFR. The intracellular processes triggered by activation of EGFR (dimerization, autophosphorylation and signal transduction) are prevented by panitumumab, leading ultimately to increased apoptosis, reduced proliferation of tumour cells and reduced angiogenesis. Tumour growth and development of metastases are prevented.

Adverse effects

The most common adverse effects include eye, skin and gastrointestinal problems, which are related to the primary mode of action through the blockade of the EGFR. Hypomagnesaemia, another common problem, can be explained by effects of panitumumab on tubular reabsorption of filtered magnesium in the kidney and on magnesium absorption in the gastrointestinal tract.

Literature

Easley C, Kirkpatrick P. FRESH FROM THE PIPELINE: Panitumumab. Nat Rev Drug Discov 2006; 5: 987–8.

Imai K, Takaoka A. Comparing antibody and small-molecule therapies for cancer. Nat Rev Cancer 2006; 6: 714–27.

Available at http://www.emea.europa.eu/humandocs/Humans/EPAR/vectibix/vectibix.htm

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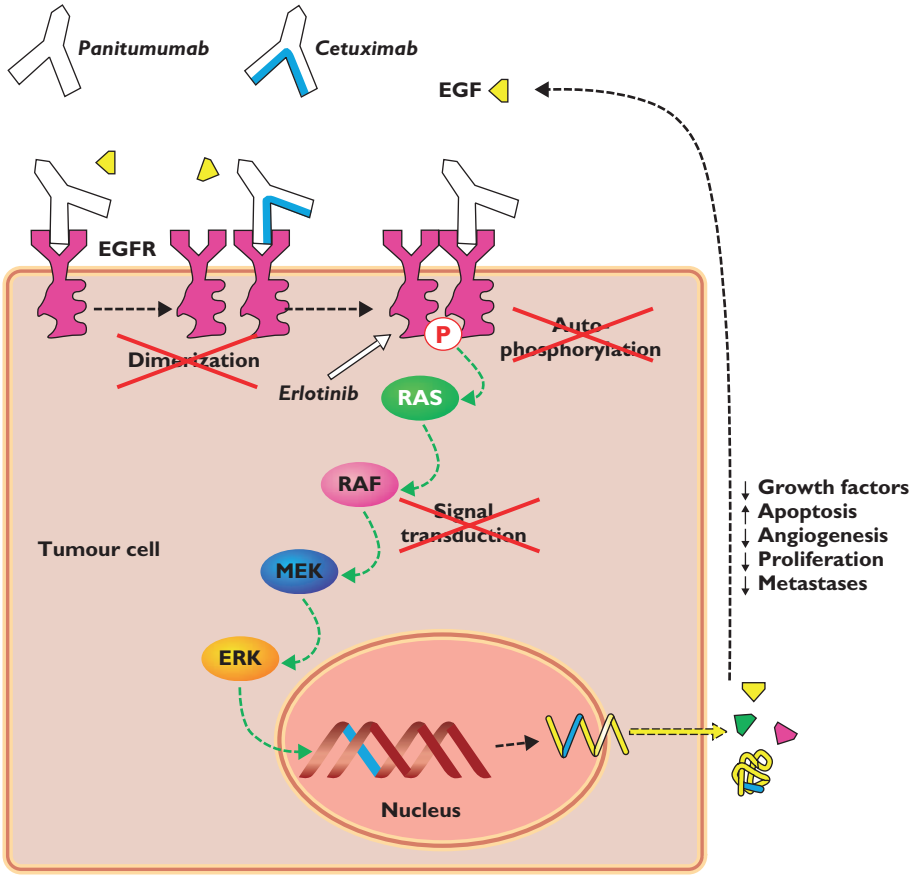

Panitumumab blocks the epidermal growth factor receptor (EGFR) preventing EGF and other growth factors from binding. Activation of the EGFR and the subsequent cascade of signal transduction are inhibited, resulting in decreased expression of growth factors. Cetuximab and erlotinib also prevent activation of the EGFR