Panitumumab

Panitumumab (INN), formerly **ABX-EGF**, is a fully human monoclonal antibody specific to the epidermal growth factor receptor (also known as *EGF receptor*, *EGFR*, *ErbB-1* and *HER1* in humans).

Panitumumab is manufactured by Amgen and marketed as **Vectibix**. It was originally developed by Abgenix Inc.

In 2014, Amgen and Illumina entered into an agreement to develop a companion diagnostic to accompany panitumumab.[1]

1 Uses

It was approved by the U.S. Food and Drug Administration (FDA) for the first time in September 2006, for "the treatment of EGFR-expressing metastatic colorectal cancer with disease progression" despite prior treatment.[2] Panitumumab was approved by the European Medicines Agency (EMEA) in 2007, and by Health Canada in 2008 for "the treatment of refractory EGFR-expressing metastatic colorectal cancer in patients with non-mutated (wild-type) KRAS".

Panitumumab was the first monoclonal antibody to demonstrate the use of KRAS as a predictive biomarker.

2 FDA Approval

Panitumumab was initially approved on September 27, 2006 for EGFR-expressing, metastatic CRC with disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing regimens, based on the results of a study which showed clinical benefit in metastatic colorectal cancer patients.[3] In July 2009, the FDA updated the labels of two anti-EGFR monoclonal antibody drugs (panitumumab and cetuximab) indicated for the treatment of metastatic colorectal cancer to include information about KRAS mutations.[4] This was the result of a study, which demonstrated lack of benefit with Panitumumab in patients who carried NRAS mutations.[5]

3 Mechanism

Main article: Epidermal growth factor receptor

EGFR is a transmembrane protein. Panitumumab works by binding to the extracellular domain of the EGFR preventing its activation. This results in halting of the cascade of intracellular signals dependent on this receptor.[6]

4 Development and production

Panitumumab was developed by immunization of transgenic mice (XenoMouse) that are able to produce human immunoglobulin light and heavy chains. After immunization of these animals a specific clone of B cells that produced an antibody against EGFR was selected and immortalized in Chinese hamster ovary (CHO) cells. These cells are then used for the full scale manufacture of the 100% human antibody.

5 Pharmacokinetics

The pharmacokinetics (PK) of panitumumab shows the so-called target-mediated disposition behavior.[7] However, the PK is approximately linear at clinical doses, and the terminal half-life for a typical male patient of 80 kg and 60 years of age with colorectal cancer is about 9.4 days.

6 Side Effects

Panitumumab, like cetuximab has been associated with skin rash, fatigue, nausea, diarrhea and decreased magnesium levels. Often, skin rash is noted in the sun exposed parts of the body, such as the face or chest. Oral antibiotics may be needed for worsening skin rash, such as one accompanied with blisters and ulcers. Otherwise, topical steroid creams like hydrocortisone may help.[8]

7 Contraindications

Panitumumab does not work in patients who have KRAS or NRAS mutations.[5] It does not have a role in the treatment of adjuvant treatment of colon or rectal cancer. A severe reaction to panitumumab infusion is also concerning, and further exposure to the drug should be avoided.

8 Panitumumab vs. Cetuximab

Although they both target the EGFR, panitumumab (IgG2) and cetuximab (IgG1) differ in their isotype and they might differ in their mechanism of action. Monoclonal antibodies of the IgG1 isotype may activate the complement pathway and mediate antibody-dependent cellular cytotoxicity (ADCC).[9] It is not clear at this time, if one drug is superior to the other. In one of the studies, both these drugs were noted to be similar in activity.[10]

9 References

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10 Further reading

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