Diese Meldung kann unter http://www.presseportal.de/meldung/2068248/ abgerufen werden.

Amgen

Amgen Receives Positive CHMP Opinion for Vectibix® (Panitumumab) in Combination With Chemotherapy

24.06.2011 - 17:42 Uhr, Amgen

Thousand Oaks, California (ots/PRNewswire) - Amgen today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending that Vectibix(R) (panitumumab) be approved for use in the European Union (EU) in first-line in combination with FOLFOX and in second-line in combination with FOLFIRI in patients who have received first-line fluoropyrimidine-based chemotherapy (excluding irinotecan) for patients with wild-type KRAS metastatic colorectal cancer (mCRC), following a successful re-examination procedure by Amgen.

"This opinion, for which a final European Commission decision is pending, is a welcome step forward and one that may lead to additional treatment options for patients facing an aggressive disease with limited treatment options," said Willard H. Dere, M.D., senior vice president and international chief medical officer at Amgen. "Studies have shown that patients taking Vectibix in combination with chemotherapy have a greater chance of living longer without their disease getting worse, in a landscape where few targeted agents have been shown to be effective when used with chemotherapy."

Data from studies 20050203 (PRIME) and 20050181 ('181) showed that adding Vectibix to either FOLFOX or FOLFIRI chemotherapy improved progression-free survival (PFS) versus chemotherapy alone for patients with wild-type KRAS mCRC. Additionally, the overall response rate (ORR) of Vectibix plus chemotherapy was higher than chemotherapy alone. Although numerically greater, the improvement in median overall survival (OS) did not achieve statistical significance in the Vectibix arm of either trial.(i)

The PRIME study evaluated Vectibix (6.0 mg/kg every two weeks) plus FOLFOX versus FOLFOX alone in patients with wild-type KRAS mCRC and found that Vectibix plus FOLFOX significantly improved PFS versus FOLFOX alone (median 9.6 months versus 8.0 months, hazard ratio (HR) 0.80; 95 percent confidence interval (CI): 0.66-0.97; p=0.02).(i) Additionally, combining Vectibix with FOLFOX resulted in numerically greater OS versus FOLFOX alone (median 23.9 months versus 19.7 months, HR 0.83; 95 percent CI: 0.67-1.02), although this was not statistically significant (p=0.072).(i) The ORR achieved with Vectibix plus FOLFOX was higher than FOLFOX alone (55 percent versus 48 percent).(i)

The '181 study showed that adding Vectibix (6.0 mg/kg every two weeks) to FOLFIRI chemotherapy improved median PFS by two months in patients with wild-type KRAS mCRC compared to FOLFIRI alone (median 5.9 months versus 3.9 months; HR 0.73, 95 percent CI: 0.59-0.90; p=0.004). Additionally, the Vectibix combination more than tripled the ORR compared to FOLFIRI alone (35 percent versus 10 percent). Though quantitatively greater (14.5 months versus 12.5 months, HR 0.85), the improvement in median OS (co-primary endpoint) did not achieve statistical significance in the Vectibix arm of the trial (p=0.12).(ii)

Adverse event rates included known toxicities associated with anti-epidermal growth factor receptor (EGFR) therapy, such as rash, diarrhea, and hypomagnesemia. Vectibix-related grade 3/4 infusion reactions were reported in less than one percent of patients.(i) In patients with mutated KRAS tumors, outcomes were inferior for those receiving Vectibix plus FOLFOX versus FOLFOX alone.(ii iii) Vectibix should only be used in those patients in whom wild-type KRAS status has been confirmed, because of the worse outcomes in patients with mutated KRAS tumors treated with FOLFOX.

The Amgen PRIME and '181 studies were the first Phase 3 studies to prospectively analyze the effect of an EGFR inhibitor based on KRAS status in patients with mCRC.

Vectibix is already approved and established in 40 countries as a monotherapy treatment for patients with wild-type KRAS mCRC, when standard chemotherapy is no longer effective. In the United States (U.S.), Vectibix received accelerated approval in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. The use of Vectibix is not recommended in patients whose tumors have KRAS mutations in codon 12 or 13. In Japan and Israel, Vectibix is also approved for use in combination with chemotherapy for patients with wild-type KRAS mCRC.

About KRAS

Results from studies performed over the last 25 years indicate that KRAS plays an important role in cell growth regulation. In mCRC, EGFR transmits signals through a set of

intracellular proteins. Upon reaching the nucleus, these signals instruct the cancer cell to reproduce and metastasize, leading to cancer progression.(iv) Anti-EGFR antibody therapies work by inhibiting the activation of EGFR, thereby inhibiting downstream events that lead to malignant signaling. However, in patients whose tumors harbor a mutated KRAS gene, the KRAS protein is always turned "on," regardless of whether the EGFR has been activated or therapeutically inhibited. KRAS mutations occur in approximately 40 to 50 percent of mCRC patients.(v vi)

About Colorectal Cancer

Colorectal cancer is the third most common cancer worldwide in men and the second most common in women. In 2008, approximately 1.23 million cases of colorectal cancer were diagnosed globally.(vii) In 2008, there were an estimated 333,330 new cases of colorectal cancer in the EU.(viii)

About Vectibix

Vectibix is the first fully human anti-EGFR antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of mCRC. Vectibix was approved in the U.S. in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

The effectiveness of Vectibix as a single agent for the treatment of EGFR-expressing mCRC is based on PFS. More than half of patients who receive Vectibix monotherapy respond to treatment with an average six month PFS benefit. Currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix.

Retrospective subset analyses of mCRC trials have not shown a treatment benefit for Vectibix in patients whose tumors had KRAS mutations in codon 12 or 13. Use of Vectibix is not recommended for the treatment of mCRC with these mutations.(ix)

In December 2007, the European Commission granted a conditional marketing authorization for Vectibix as a monotherapy for the treatment of patients with EGFR-expressing mCRC with non-mutated (wild-type) KRAS after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.(x) Vectibix has been launched in more than 30 European countries, Russia, Israel, Australia, Canada and Japan. Applications in the rest of the world are pending.

Important U.S. Product Safety Information

WARNING: DERMATOLOGIC TOXICITY and INFUSION REACTIONS

Dermatologic Toxicity: Dermatologic toxicities occurred in 89 percent of patients and were severe (NCI-CTC grade 3 or higher) in 12 percent of patients receiving Vectibix monotherapy. [See Dosage and Administration (2.1), Warnings and Precautions (5.1), and Adverse Reactions (6.1)].

Infusion Reactions: Severe infusion reactions occurred in approximately one percent of patients. Fatal infusion reactions occurred in postmarketing experience [See Dosage and Administration (2.1), Warnings and Precautions (5.2), and Adverse Reactions (6.1, 6.3)].

The most common adverse events of Vectibix are skin rash with variable presentations, hypomagnesemia, paronychia, fatigue, abdominal pain, nausea, and diarrhea, including diarrhea resulting in dehydration.

Important European Product Safety Information

For full prescribing information please see the Summary of Product Characteristics.

Vectibix is indicated as monotherapy for the treatment of patients with EGFR-expressing, mCRC with nonmutated (wild-type) KRAS after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

Vectibix is contraindicated in patients with a history of severe or life-threatening hypersensitivity reactions to the product and in patients with interstitial pneumonitis or pulmonary fibrosis.

Other common adverse events of special importance associated with Vectibix and/or EGFR monoclonal antibody therapies include dermatologic-related reactions, pulmonary complications, electrolyte disturbances and infusion-related reactions (including rare reports with fatal outcome). These events should be monitored carefully, see Summary of Product Characteristics for information on appropriate management of these adverse events. Acute renal failure has been observed in patients who develop severe diarrhoea and dehydration.

Vectibix should not be used in combination with IFL [bolus 5-fluorouracil (500 mg/m2), leucovorin (20 mg/m2) and irinotecan (125 mg/m2)] or in combination with bevacizumab containing chemotherapy.

Vectibix should not be administered in combination with oxaliplatin-containing chemotherapy to mCRC patients with mutant KRAS tumors or for whom KRAS tumor status is unknown.

About Amgen

Amgen discovers, develops, manufactures and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, bone disease and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit http://www.amgen.com.

Forward-Looking Statements

This news release contains forward-looking statements that are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and most recent periodic reports on Form 10- Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of June 24, 2011 and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and products liability claims. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations.

The scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. FDA, European Medicines Agency (EMA) or similar regulatory bodies for the products.

The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses. Only the FDA, EMA or similar regulatory bodies can determine whether the products are safe and effective for these uses. Healthcare professionals should refer to and rely upon the approved labeling for the products, and not the information discussed in this news release.

CONTACT: Amgen Carrie Deverell: +41-41-3690-308 (E.U. media) Christine Regan: +1-805-447-5476 (U.S. media) Arvind Sood: +1-805-447-1060 (investors)

(Logo http://photos.prnewswire.com/prnh/20081015/AMGENLOGO)

(i) 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 28, 2010.

(ii) Adverse event rates were comparable across arms with the exception of known toxicities associated with EGFR therapy such as rash, diarrhea and hypomagnesemia. Vectibix-related grade 3 infusion reactions were reported for two patients (less than one percent).

(iii) In general, adverse events rates were comparable across arms with the exception of known toxicities associated with anti-epidermal growth factor receptor (EGFR) therapy such as rash, diarrhea, and hypomagnesemia. Vectibix-related grade 3/4 infusion reactions were reported in less than one percent of patients.

(iv) Malumbres, M. and Barbacid, M. RAS oncogenes: the first 30 years. Nature Reviews Cancer. 3:459-65, 2003.

(v) Karapentis C, S. Snell, L, E. The Laboratory Assessment of KRAS Mutation Status in Colorectal Cancer. Asia, Pacific Journal of Oncology and Hematology. 2010.

(vi) Friday BB and Adjei AA. K-ras as a target for cancer therapy. Biochim. Biophys. Acta 1756: 127-144, 2005

(vii) Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10. Lyon, France: International Agency for Research on Cancer; 2010

(viii) Ferlay J, Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer. 2010 Mar; 46(4):765-81. Epub 2010 Jan 29.

(ix) Vectibix (panitumumab) [prescribing information]. Thousand Oaks, Calif: Amgen; 2011.

(x) Vectibix (panitumumab) SPC. Thousand Oaks, Calif: Amgen; 2011

Contact:
.

Original text: Amgen
Digitale Pressemappe: http://www.presseportal.de/pm/73691/
Pressemappe via RSS: http://presseportal.de/rss/pm_73691.rss2