New England Journal of Medicine Study Shows ERBITUX® Improves Survival in Advanced Colorectal Cancer

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Terms:
- First Study to Demonstrate Survival Benefit with ERBITUX in Patients with Colorectal Cancer Refractory to All Approved Chemotherapies -

NEW YORK--(BUSINESS WIRE)--ImClone Systems Incorporated (NASDAQ: IMCL) and Bristol-Myers Squibb Company (NYSE: BMY) announced today results from a multicenter, open-label, randomized Phase III trial, published in the New England Journal of Medicine, in which ERBITUX® (cetuximab) as a single agent demonstrated a significant improvement in overall survival in patients with metastatic colorectal cancer (mCRC) refractory to approved chemotherapy agents. The study compared ERBITUX plus best supportive care (BSC) to BSC alone in patients with mCRC whose disease had progressed through treatment with all approved chemotherapy, including irinotecan, oxaliplatin, and fluoropyrimidines.

The independent study (NCIC CTG CO.17), conducted by the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) in collaboration with the Australasian Gastro-Intestinal Trials Group (AGITG), involved 572 patients and demonstrated that treating patients with ERBITUX as a monotherapy plus BSC significantly increased overall survival compared to BSC alone. BSC included palliative therapies designed to alleviate pain and treat other effects caused by mCRC.

"This is the first time an antibody used as a single agent in colorectal cancer has demonstrated an overall survival benefit. These outcomes add to the growing body of evidence supporting the significant clinical benefits of ERBITUX," said Eric K. Rowinsky, M.D., Chief Medical Officer and Senior Vice President of ImClone Systems.

"These data demonstrate that ERBITUX may provide certain colorectal cancer patients with additional time -- even when other available treatment options have failed," said Maurizio Voi, M.D., Executive Director, Oncology Global Medical Affairs, Bristol-Myers Squibb. "The results are part of our comprehensive clinical development program designed to fully understand the potential uses of ERBITUX."

The study enrolled patients with epidermal growth factor receptor (EGFR)-expressing metastatic colorectal cancer who had been previously treated. ERBITUX was administered at the recommended dose and schedule: 400 mg/m2 initial dose, followed by 250 mg/m2 weekly until disease progression or unacceptable toxicity.

In this study, the median survival was 6.1 months for patients treated with ERBITUX plus BSC versus 4.6 months for patients on BSC alone (Hazard Ratio: 0.77, P=0.005). Treatment with ERBITUX monotherapy resulted in a significant improvement in progression-free survival versus BSC alone (Hazard Ratio: 0.68, P<0.001). Twenty-three patients (8.0%) treated with ERBITUX and no patients on BSC alone had partial responses (P<0.001).

Grade 3/4 adverse events (occurring in greater than or equal to 10% of patients in either group) reported more frequently in the ERBITUX plus BSC treatment arm compared with the BSC only arm included fatigue (33% vs 26%), other pain (16% vs 7%), dyspnea (16% vs 12%), infection without neutropenia (13% vs 6%) rash/desquamation (12% vs <1%), and other gastrointestinal (10% vs 8%). Grade 3/4 infusion reactions (hypersensitivity) occurred in 5% of patients in the ERBITUX plus BSC arm. The most common (occurring in greater than or equal to 25% of patients in either group) adverse events of any grade were rash/desquamation, fatigue, abdominal pain, other pain, dry skin, dyspnea, constipation, pruritus, diarrhea, vomiting, infection without neutropenia, headache, fever, insomnia, cough, other dermatology, and stomatitis.

This study supported the recent label change for ERBITUX -- approved by the U.S. Food and Drug Administration on October 2, 2007 -- to include overall survival data as a monotherapy agent in patients with EGFR-expressing mCRC after failure of irinotecan- and oxaliplatin-based chemotherapy regimens.

About Colorectal Cancer

In the U.S., approximately 154,000 people will be diagnosed with cancer of the colon or rectum this year. More than half of these patients have metastatic disease, or cancer that has spread to other organs, at the time of diagnosis. EGFR is expressed in 60-80 percent of colorectal cancer tumors. Colorectal cancer is the third most common cancer in both men and women, excluding skin cancer.

About ERBITUX® (cetuximab)

ERBITUX is a monoclonal antibody (IgG1 Mab) designed to inhibit the function of a molecular structure expressed on the surface of normal and tumor cells called the epidermal growth factor receptor (EGFR, HER1, c-ErbB-1). In vitro assays and in
vivo animal studies have shown that binding of ERBITUX to the EGFR blocks phosphorylation and activation of receptor-associated kinases, resulting in inhibition of cell growth, induction of apoptosis, and decreased matrix metalloproteinase and vascular endothelial growth factor production. In vitro, ERBITUX can mediate antibody-dependent cellular cytotoxicity (ADCC) against certain human tumor types. No anti-tumor effects of ERBITUX were observed in human tumor xenografts lacking EGFR expression. EGFR is part of a signaling pathway that is linked to the growth and development of many human cancers, including those of the head and neck, colon and rectum.

ERBITUX, as a single agent, is indicated for the treatment of EGFR-expressing mCRC after failure of both irinotecan- and oxaliplatin-based regimens. ERBITUX, as a single agent, is also indicated for the treatment of EGFR-expressing mCRC in patients who are intolerant to irinotecan-based regimens.

For full prescribing information, including boxed WARNINGS regarding infusion reactions and cardiopulmonary arrest, visit [http://www.erbitux.com/](http://www.erbitux.com/).

**Important Safety Information**

**Grade 3/4 infusion reactions** occurred in approximately 3% of patients receiving ERBITUX (Cetuximab) in clinical trials with fatal outcome reported in less than 1 in 1000. Reactions characterized by rapid onset of airway obstruction (bronchospasm, stridor, hoarseness), urticaria, hypotension, loss of consciousness, and/or cardiac arrest. Severe infusion reactions require immediate and permanent discontinuation of ERBITUX therapy.

Most reactions (90%) were associated with the first infusion of ERBITUX despite premedication with antihistamines. Caution must be exercised with every ERBITUX infusion as there were patients who experienced their first severe infusion reaction during later infusions. Monitor patients for 1-hour following ERBITUX infusions in a setting with resuscitation equipment and other agents necessary to treat anaphylaxis (e.g., epinephrine, corticosteroids, intravenous antihistamines, bronchodilators, and oxygen). Longer observation periods may be required in patients who require treatment for infusion reactions.

Severe cases of interstitial lung disease (ILD), which was fatal in one case, occurred in 4 of 1570 (<0.5%) of patients receiving ERBITUX in clinical trials. Permanently discontinue ERBITUX where ILD is confirmed.

In clinical studies of ERBITUX, dermatologic toxicities, including acneform rash, skin drying and fissuring, paronychial inflammation, infectious sequelae (e.g., Staphylococcus aureus sepsis, abscess formation, cellulitis, blepharitis, cheilitis), and hypertrichosis occurred in patients receiving ERBITUX therapy. Acneform rash occurred in 76-88% of 1373 patients receiving ERBITUX in clinical trials with severe acneform rash occurring in 1-17% of patients. Acneform rash usually developed within the first 2 weeks of therapy and resolved in a majority of the patients after cessation of treatment, although in nearly half, the event continued beyond 28 days. Monitor patients receiving ERBITUX for dermatologic toxicities and infectious sequelae. Sun exposure may exacerbate these effects.

In women of childbearing potential, appropriate contraceptive measures must be used during treatment with ERBITUX and for 6 months following the last dose of ERBITUX. If ERBITUX is used during pregnancy or if patients become pregnant while receiving ERBITUX, patients should be apprised of the potential risk for loss of pregnancy or potential hazard to the fetus.

Hypomagnesemia occurred in 55% (199/365) of patients receiving ERBITUX and was severe (NCI CTC grades 3 & 4) in 6-17%. The onset of hypomagnesemia and accompanying electrolyte abnormalities occurred days to months after initiation of ERBITUX. Monitor patients periodically for hypomagnesemia, hypocalcemia and hypokalemia, during and for at least 8 weeks following the completion of ERBITUX. Replete electrolytes as necessary.

The most serious adverse reactions associated with ERBITUX in mCRC patients are infusion reactions, dermatologic toxicity, sepsis, renal failure, interstitial lung disease, and pulmonary embolus.

The most common adverse reactions with ERBITUX (incidence greater than or equal to 25% in the ERBITUX + plus best supportive care arm (BSC) (n=288) vs. BSC (n=274), respectively, were fatigue (89%, 76%), rash/desquamation (89%, 16%), abdominal pain (59%, 52%), pain-other (51%, 34%), dry skin (49%, 11%), dyspnea (48%, 43%), constipation (46%, 38%), pruritus (40%, 8%), diarrhea (39%, 20%), vomiting (37%, 29%), infection without neutropenia (35%, 17%), headache (33%, 11%), fever (30%, 18%), insomnia (30%, 15%), cough (29%, 19%), dermatology-other (27%, 6%), and stomatitis (25%, 10%).

**About ImClone Systems**

ImClone Systems Incorporated is a fully integrated biopharmaceutical company committed to advancing oncology care by developing and commercializing a portfolio of targeted biologic treatments designed to address the medical needs of patients with a variety of cancers. The Company’s research and development programs include growth factor blockers and angiogenesis inhibitors. ImClone Systems’ headquarters and research operations are located in New York City, with additional administration and manufacturing facilities in Branchburg, New Jersey. For more information about ImClone Systems, please visit the Company’s web site at [http://www.imclone.com/](http://www.imclone.com/).

ERBITUX® is a registered trademark of ImClone Systems Incorporated.

Certain matters discussed in this news release may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and the Federal securities laws. Although the company believes that the expectations reflected in such forward-looking statements are based upon reasonable assumptions it can give no assurance that its expectations will be achieved. Forward-looking information is subject to certain risks, trends and uncertainties that could cause actual results to differ materially from those currently expected. Many of these factors are beyond the company’s ability to control or predict. Important factors that may cause actual results to differ materially and could impact the company and the statements contained in this news release can be found in the company’s filings with the Securities and Exchange Commission, particularly those factors identified as “risk factors” in the Company’s most recent annual report.
of Form 10-K and in its quarterly reports on Form 10-Q and current reports on Form 8-K. For forward-looking statements in this news release, the company claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. The company assumes no obligation to update or supplement any forward-looking statements whether as a result of new information, future events or otherwise.

About Bristol-Myers Squibb

Bristol-Myers Squibb is dedicated to the discovery, development and exhaustive exploration of innovative cancer fighting therapies that extend and enhance the lives of patients living with cancer. More than 40 years ago, Bristol-Myers Squibb built a unified vision for the future of cancer treatment. With expertise, dedication and resolve, that vision led to the development of a diverse global portfolio of anti-cancer therapies that are an important cornerstone of care today. Hundreds of scientists in Bristol-Myers Squibb’s Research & Development organization are studying ways to improve current cancer treatments and identify better, more effective medicines for the future.

Bristol-Myers Squibb is a global pharmaceutical and related health care products company whose mission is to extend and enhance human life.

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb’s business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2006, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

SOURCE: Bristol-Myers Squibb; ImClone Systems Incorporated

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