

Basel, 28 January 2008

Avastin receives broad label extension in Europe for the treatment of patients with metastatic colorectal cancer

Many more patients can now benefit from Avastin's proven survival benefits

Roche announced today that the European Commission (EC) has given its approval for the significantly wider use of its anti-angiogenic agent Avastin (bevacizumab) in patients suffering from metastatic colorectal cancer.

This new broader label will now allow Avastin to be used in combination with any chemotherapy, including Roche's oral chemotherapy Xeloda (capecitabine), for 1st and later treatment lines in patients with metastatic colorectal cancer. This news means that virtually all patients with metastatic colorectal cancer now have access to Avastin's proven survival benefits. It is estimated that more than 400,000 people in Europe will be diagnosed with metastatic colorectal cancer in 2008.ⁱ

The Avastin approval follows the European Committee for Medicinal Products for Human Use (CHMP) positive recommendations for the extended use of both Avastin and Xeloda in December 2007. The final EC decision on Xeloda for its extended use is expected imminently.

The new Avastin label will allow it to be used in combination with every standard fluoropyrimidine based chemotherapy and also allows for combinations with Xeloda or oxaliplatin. Avastin formerly could only be used in combination with IV 5-FU or IV 5-FU/irinotecan-based chemotherapy regimenⁱⁱ where it had demonstrated an impressive survival extension of nearly 5 months. Physicians now have the flexibility to use Avastin with a broad variety of standard chemotherapy of their choice in any line of metastatic colorectal cancer.

“This news is highly significant for the estimated 400,000 people diagnosed with metastatic colorectal cancer every year in Europe alone” said William M. Burns, member of the Executive Committee and CEO of the Pharmaceuticals Division at Roche. “This is another milestone in our commitment to developing effective and safe treatments for the large number of colorectal cancer patients throughout the world.”

The approval of this broad label is based on the results of two large international phase III pivotal studies (NO16966 and E3200).

“This is a major turning point in the treatment of metastatic colorectal cancer patients," said Professor Alberto Sobrero, Head of Medical Oncology, Hospital San Martino, Genoa, Italy. “This approval means that many more patients can benefit from Avastin’s significant survival benefits.”

About the Phase III studies that formed the basis of the approval

Note: Progression-free survival is a measure of the time patients live without their disease advancing.

NO16966 study

NO16966 is a large, international phase III trial which recruited 2,034 patients. It was originally planned to compare XELOX vs FOLFOX as first-line treatment in metastatic colorectal cancer. After release of the pivotal Avastin data in colorectal cancer in 2003, the protocol was amended to investigate using a 2 by 2 factorial design: FOLFOX/XELOX + placebo vs FOLFOX/XELOX + Avastin.

The primary objective was to answer two questions: 1) whether the XELOX regimen is non-inferior to FOLFOX; 2) whether the addition of Avastin to chemotherapy improved progression-free survival compared to chemotherapy alone. The secondary endpoints included overall survival, overall response rates, time to, and duration of, response and safety profile. Results of the study showed:

- The addition of Avastin to chemotherapy (XELOX or FOLFOX-4) significantly improved progression-free survival by 20% compared with chemotherapy alone.
- In patients that received treatment until disease progression, the benefit was even greater, and adding Avastin to chemotherapy improved progression-free survival by 58%.
- The chemotherapy combination XELOX is as effective in terms of progression-free survival as FOLFOX.

E3200 study

The E3200 study is a randomized, controlled, multi-center phase III trial of 829 patients with

advanced or metastatic colorectal cancer who had received previous treatment with irinotecan and 5-FU as initial therapy for metastatic disease or as adjuvant therapy. The study showed that patients who received Avastin plus the 5-FU-based chemotherapy regimen known as FOLFOX4 (oxaliplatin/5-FU/leucovorin) had a 25 percent reduction in the risk of death (based on a hazard ratio of 0.75), the primary endpoint, which is equivalent to a 33 percent improvement in overall survival, compared to patients who received FOLFOX4 alone. Median survival for patients receiving Avastin plus FOLFOX4 was 12.9 months, compared to 10.8 months for those receiving FOLFOX4 alone.

About Avastin

Data from the comprehensive Avastin cancer clinical development programme have resulted in approvals in advanced colorectal, breast, lung, and kidney cancer:

- February 2004 (US) and January 2005 (EU) – first-line treatment in patients with metastatic colorectal cancer (CRC)
- June 2006 (US) – second-line treatment in patients with metastatic CRC
- October 2006 (US) – first-line treatment in patients with advanced non-small cell lung cancer (NSCLC)
- March 2007 (EU) – first-line treatment in patients with metastatic breast cancer
- April 2007 (Japan) – treatment in patients with recurrent or advanced CRC
- August 2007 (EU) – first-line treatment in patients with advanced NSCLC
- December 2007 (EU) – first-line treatment in patients with advanced RCC

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, a market leader in virology and active in other major therapeutic areas such as autoimmune diseases, inflammation, metabolic disorders and diseases of the central nervous system. In 2006, sales by the Pharmaceuticals Division totalled 33.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.7 billion Swiss francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invests approximately 7 billion Swiss francs a year in R&D. Worldwide, the Group employs about 75,000 people. Additional information is available on the Internet at www.roche.com.

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Additional information

- Roche in Oncology: www.roche.com/pages/downloads/company/pdf/mboncology05e_b.pdf
- Roche Health Kiosk, Cancer: www.health-kiosk.ch/start_krebs
- Avastin: www.avastin-info.com

To access video clips about Avastin and Xeloda, in broadcast standard, free of charge, please go to:
www.thenewsmarket.com.

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References

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ⁱⁱ Hurwitz H, Fehrenbacher L, Novotny W et al. Addition of bevacizumab (rhuMab-VEGF) to bolus IFL in the first-line treatment of patients with metastatic colorectal cancer: results of a randomized Phase III trial. *New England Journal of Medicine* 2004; 350(23): 2335–42.