FDA approves new use of Avastin plus chemotherapy for people with metastatic colorectal cancer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has approved a new use of Avastin (bevacizumab) in combination with fluoropyrimidine-based irinotecan or oxaliplatin chemotherapy for people with metastatic colorectal cancer (mCRC). The new indication will allow people who received Avastin plus an irinotecan or oxaliplatin containing chemotherapy as an initial treatment (first-line) for mCRC to continue to receive Avastin plus a different irinotecan or oxaliplatin containing chemotherapy after their cancer worsens (second-line treatment).

“The majority of people diagnosed with metastatic colorectal cancer receive Avastin plus chemotherapy as their initial treatment,” said Hal Barron, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “These people now have the option to continue with Avastin plus a new chemotherapy after their cancer worsens, which may help them live longer than changing to the new chemotherapy alone.”

Avastin in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy is now indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line Avastin-containing regimen. The approval is based on positive results from the Phase III ML18147 study, which were presented at the 2012 American Society of Clinical Oncology annual meeting and showed that people who continued to receive an Avastin-based regimen after their cancer worsened lived longer than people who switched to chemotherapy alone.

Avastin is the only biologic medicine approved by the FDA to treat people with mCRC in combination with intravenous 5FU-based chemotherapy as an initial treatment, as treatment for people whose cancer has worsened after chemotherapy alone, and now as a treatment for people whose cancer has worsened after initial treatment with an Avastin-based regimen. This is the third approval for Avastin in mCRC based on improved overall survival. Avastin is not indicated for adjuvant treatment of colon cancer.
Avastin is approved in Europe in combination with fluoropyrimidine-based chemotherapy for the treatment of adult patients with metastatic carcinoma of the colon or rectum. The European product information has been updated based on the positive results of the Phase III ML18147 study with an implementation date of December 12, 2012 allowing people with mCRC who received Avastin plus chemotherapy as a first-line treatment to continue to receive Avastin plus chemotherapy after their cancer worsens as part of their second-line treatment.

About the ML18147 study
ML18147 was a randomised, open-label, phase III, multicentre, multinational trial evaluating the efficacy and safety profile of Avastin plus standard second-line chemotherapy in 820 patients with mCRC whose disease had progressed following Avastin plus standard first-line chemotherapy (irinotecan or oxaliplatin-based). Patients were randomised at progression to one of two treatment arms:

- Arm A: chemotherapy* plus Avastin (equivalent of 2.5 mg/kg i.v. per week)
- Arm B: chemotherapy* alone

*Depending on the first-line chemotherapy backbone (fluoropyrimidine/irinotecan-based or fluoropyrimidine/oxaliplatin-based), the chemotherapy backbone was switched in the second-line setting.

- The risk of death was reduced by 19 percent for people who received Avastin in combination with standard chemotherapy in both the first- and second-line compared to those who received chemotherapy alone (HR=0.81, p= 0.0057). Median overall survival was 11.2 months compared to 9.8 months.
- The risk of the cancer worsening or death (progression-free survival; PFS) was reduced by 32 percent (HR=0.68, p<0.0001). Median PFS was 5.7 months compared to 4.1 months.
- There was no significant difference in response rate between treatment arms.
- Overall survival and PFS were calculated from the time patients were randomised to the second-line treatment.
- Adverse events (AEs) in ML18147 were consistent with those seen in previous pivotal trials of Avastin in mCRC.

The primary endpoint of the study was overall survival measured from the time patients were randomized to the second-line treatment. The secondary efficacy endpoints of the study included PFS, overall response rate and safety profile.
About colorectal cancer

Colorectal cancer is one of the most common cancers in the world, with over 1.2 million new cases diagnosed each year\(^1\) and it remains one of the biggest cancer killers in the world responsible for over 600,000 deaths globally each year.\(^1\)

About Avastin – over 8 Years of transforming cancer care

With the initial approval in the USA for advanced colorectal cancer in 2004, Avastin became the first anti-angiogenic therapy made widely available for the treatment of patients with an advanced cancer.

Today, Avastin is continuing to transform cancer care through its proven survival benefit (overall survival and/or progression free survival) across several types of cancer. Avastin is approved in Europe for the treatment of advanced stages of breast cancer, colorectal cancer, non-small cell lung cancer, kidney cancer and ovarian cancer, and is available in the US for the treatment of colorectal cancer, non-small cell lung cancer and kidney cancer. In addition, Avastin is approved in the US and almost 40 other countries worldwide for the treatment of patients with progressive glioblastoma following prior therapy. Avastin is approved in Japan for the treatment of the advanced stages of colorectal, non-small cell lung cancer and breast cancer. Avastin is the only anti-angiogenic therapy available for the treatment of these numerous advanced cancer types, which collectively cause over 2.5 million deaths each year.

Avastin has made anti-angiogenic therapy a fundamental pillar of cancer treatment today. Over one million patients have been treated with Avastin so far. A comprehensive clinical programme with more than 500 ongoing clinical trials is investigating the use of Avastin in over 50 tumour types.

About Avastin – mode of action

An independent blood supply is critical for a tumour to grow beyond a certain size (2mm) and spread (metastasise) to other parts of the body. Tumours develop their own blood supply in a process called angiogenesis by releasing vascular endothelial growth factor (VEGF) – a key driver for tumour growth. Avastin is an antibody that precisely targets and inhibits VEGF for continuous tumour control. Precise VEGF inhibition by Avastin allows it to be combined effectively with a broad range of chemotherapies and other anti-cancer treatments with limited additional impact on the side effects of these therapies.
About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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Additional information

- Roche in Oncology: www.roche.com/media/media_backgrounder/media_oncology.htm

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\(^1\) WHO, IARC GLOBOCAN, Cancer Incidence and Mortality Worldwide in 2008 at http://globocan.iarc.fr/