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FDA grants accelerated approval of Avastin in combination with paclitaxel chemotherapy for first-line treatment of patients with advanced HER2-negative breast cancer

Avastin now approved for the three cancers with the highest death toll in Europe and the US

Roche today announced that Genentech has received U.S. Food and Drug Administration (FDA) accelerated approval for Avastin (bevacizumab), in combination with paclitaxel chemotherapy, for the first-line treatment of patients with locally recurrent or metastatic breast cancer. The approval is based on a phase III study (E2100) which showed that for patients with metastatic breast cancer the addition of Avastin to paclitaxel compared to paclitaxel alone doubled the chance of being alive without the disease advancing ("progression-free survival"). In Europe Avastin received full approval for the treatment of metastatic breast cancer in March 2007.

Avastin was approved in advanced breast cancer under the FDA's accelerated approval program, which allows the FDA to approve products for cancer or other life-threatening diseases based on initial positive clinical data. Genentech has shared with the FDA a summary of the results from a second positive phase III trial (AVADO = Avastin plus docetaxel chemotherapy vs docetaxel alone), and is expecting results from a third phase III trial (RIBBON-1) in first-line metastatic breast cancer in late 2008. A full review of both the AVADO and RIBBON-1 data by the FDA will be required for the accelerated approval to be converted into a full approval. As a part of Genentech's commitment to fully evaluate Avastin in breast cancer, they will also submit data to the FDA from three additional randomized trials that are either ongoing or planned.

"This is excellent news representing a significant advancement in breast cancer therapy," said Dr David Miles, medical oncologist, Mount Vernon Hospital, UK. "The decision confirms the importance of progression-free survival as a clinically meaningful benefit to patients. Avastin effectively doubles the time patients live without their disease advancing which is highly significant for our patients and their families."

Globally, breast cancer is the second most common form of cancer and the second leading cancer killer of women with an estimated annual death toll in excess of 400,000. ⁱ

“Today’s decision represents a major milestone for patients and oncologists in the US” said William M. Burns, CEO Division Roche Pharmaceuticals. “The FDA has recognized that Avastin is a breakthrough drug which is now approved in Europe and the US for the three cancers with the highest death toll – breast, lung and colorectal cancer.”

Avastin is the first anti-angiogenic agent which has been shown to consistently deliver improved overall and/or progression-free survival benefit for colorectal, lung, breast and, renal cell cancer patients.

About E2100

The E2100 trial was sponsored by the National Cancer Institute under a Cooperative Research and Development Agreement and was conducted by a network of researchers led by the Eastern Cooperative Oncology Group (ECOG). E2100 was a multicenter, randomized and controlled clinical trial that enrolled 772 patients with previously untreated, locally recurrent or metastatic breast cancer. Patients were randomized to receive weekly treatment with paclitaxel every three out of four weeks, with or without Avastin.

Based on an independent, blinded review of patient scans, patients treated with Avastin plus paclitaxel experienced a 52 percent reduction in the risk of disease progression or death compared to those treated with paclitaxel alone (based on a hazard ratio of 0.48; $p < 0.0001$). In the Avastin arm, median PFS was 11.3 months versus 5.8 months in the paclitaxel alone arm. Based on the investigator assessment, patients treated with Avastin plus paclitaxel experienced a 58 percent reduction in the risk of disease progression or death compared to those treated with paclitaxel alone (based on a hazard ratio of 0.42; $p < 0.0001$). The data showed a similar magnitude of benefit relative to the initial results presented by ECOG at the American Society of Clinical Oncology annual meeting in 2005 and published by ECOG in the New England Journal of Medicine in 2007. The secondary endpoint of overall survival was longer in the Avastin-containing arm, as indicated by the hazard ratio of 0.87 but this improvement did not reach statistical significance ($p=0.14$). A one year exploratory analysis of overall survival was significantly improved with the addition of Avastin. (73.8% vs. 82.3%; $p=0.007$).

Safety findings were generally consistent with previous trials of Avastin plus chemotherapy and no new safety signals related to Avastin were observed. Grade 3-4 adverse events that occurred more

often in the Avastin arm included neuropathy (due to longer time on paclitaxel treatment), hypertension, arterial thromboembolic events (ATEs) and proteinuria. The incidence of hypertension, ATEs and gastrointestinal (GI) perforation in E2100 was consistent with that described in previous Avastin studies and detailed in the Avastin Prescribing Information.

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
- January 2008 (EU) – first and later-line treatment in patients with mCRC in combination with any chemotherapy
- February 2008 (US) – first-line treatment in patients with advanced breast cancer

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, and is a market leader in virology. It is also active in other major therapeutic areas such as autoimmune diseases, inflammatory and metabolic disorders and diseases of the central nervous system. In 2007 sales by the Pharmaceuticals Division totalled 36.8 billion Swiss francs, and the Diagnostics Division posted sales of 9.3 billion francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested over 8 billion Swiss francs in R&D in 2007. Worldwide, the Group employs about 79,000 people. Additional information is available on the Internet at www.roche.com.

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References

ⁱ *Parkin M, Bray F, Ferlay J, and Pisani P: CA Cancer J Clin 2005;55:74-108*