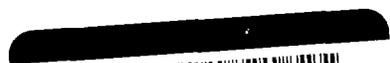


# Media release



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Basel, 15 March 2005

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## Revolutionary cancer treatment Avastin now proven to extend life also for lung cancer patients

Interim analysis shows first ever positive results in untreated patients with a biological therapy for non-small cell lung cancer

Roche and Genentech, Inc., announced today that Avastin (bevacizumab, rhuMAb-VEGF), the innovative and groundbreaking anti-angiogenesis drug, significantly improves survival in patients with advanced non-small cell lung cancer (NSCLC), the most common form of lung cancer. This is in addition to the positive results on colorectal cancer reported over the last two years.

Avastin is a unique cancer drug that works by choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body. The trial investigated the use of Avastin in patients who had not received any previous treatment - 'first line'. The interim analysis of the Phase III study investigating Avastin in combination with a platinum based chemotherapy (paclitaxel and carboplatin) met its primary efficacy endpoint of improving overall survival, or a reduction in the risk of death, compared to chemotherapy alone. The study will now be stopped since it reached its pre-specified efficacy endpoint early.

"To observe an improvement in survival in this study is remarkable, particularly as it is the first time in years that a study has shown an increase in survival for people with NSCLC in the first-line setting," said William M. Burns, CEO of Roche's Pharmaceutical Division. "These results are extremely important and we plan to share the data with the regulatory authorities in order to discuss the next steps for registering Avastin for first-line treatment of NSCLC."

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This is the first Phase III study to evaluate Avastin in combination with chemotherapy in NSCLC. This randomised, controlled, multi-centre study enrolled 878 patients with advanced NSCLC. It was sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health,

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and conducted by a network of researchers led by the Eastern Cooperative Oncology Group (ECOG). Patients were randomised to receive treatment with a platinum based chemotherapy (paclitaxel and carboplatin) with or without Avastin. The addition of Avastin to chemotherapy was well tolerated. According to ECOG, data from this study will be submitted to the annual meeting of the American Society of Clinical Oncology (ASCO), May 13 – 17.

Lung cancer is the most common cancer worldwide<sup>1</sup> with 1.2 million new cases annually and someone, somewhere dying of the disease every 30 seconds.<sup>2</sup>

#### **About the Trial**

This Phase II/III study enrolled 878 patients with advanced, non-squamous NSCLC. Patients were randomly assigned to the following arms:

Arm A: paclitaxel and carboplatin chemotherapy with placebo

Arm B: paclitaxel and carboplatin chemotherapy with Avastin

Avastin was administered at 15 mg/kg every three weeks. The paclitaxel and carboplatin chemotherapies were also administered every three weeks. Treatment in both arms repeats every three weeks for up to six courses in the absence of disease progression or unacceptable toxicity.

#### **Adverse Events**

In previous clinical experience with Avastin in combination with paclitaxel and carboplatin in NSCLC, life-threatening or fatal pulmonary bleeding was identified as a severe adverse event apparently unique to this disease. Certain characteristics, including any significant pulmonary bleeding prior to receiving treatment with Avastin or the presence of a specific type of NSCLC called squamous cell carcinoma appeared to predispose patients to experiencing this adverse event. Patients with these characteristics were excluded from this Phase III study and the rate of life-threatening or fatal pulmonary bleeding was substantially reduced from prior clinical studies. However, some patients did experience fatal pulmonary bleeding in this trial and this event was more common in the patient group that received Avastin in combination with chemotherapy than in the patient group that received chemotherapy only. Other adverse events observed in this study were similar to those identified in previous Phase II and Phase III studies of Avastin. More detailed information about adverse events in this study will be presented at the ASCO meeting in May.

#### **About Avastin**

Avastin is the first treatment that inhibits angiogenesis – the growth of a network of blood vessels that supply nutrients and oxygen to cancerous tissues. Avastin targets a naturally occurring protein

called VEGF (Vascular Endothelial Growth Factor), a key mediator of angiogenesis, thus choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis).

In Europe, Avastin is approved for first-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with the chemotherapy regimens of intravenous 5-fluorouracil/folinic acid or intravenous 5-fluorouracil/folinic acid/irinotecan. Avastin received fast-track approval by the US Food and Drug Administration (FDA) and was launched in the US in February 2004.\*

In the pivotal Phase III study, the addition of Avastin to chemotherapy (irinotecan/5-fluorouracil/leucovorin) significantly extended survival by, on average, five months (20.3 months versus 15.6 months) for people with previously untreated metastatic colorectal cancer. Avastin also significantly increased the amount of time the cancer was not growing compared with patients receiving chemotherapy alone (10.6 months vs. 6.2 months).<sup>3</sup> In a second Phase III study, conducted by the Eastern Cooperative Oncology Group (ECOG), Avastin was also shown to significantly improve survival when added to another widely prescribed chemotherapy regimen (oxaliplatin/5-fluorouracil/leucovorin). With Avastin, people who had previously failed one chemotherapy regimen for their advanced disease, lived nearly two months longer, on average, compared to those who received chemotherapy alone (12.5 months vs. 10.7 months).<sup>4</sup>

People with very advanced colorectal cancer who are too unwell to tolerate traditional aggressive chemotherapy also benefit from Avastin. The addition of Avastin to a less aggressive form of chemotherapy increased the length of time the cancer was not growing, by four months, compared to chemotherapy alone (a 67 percent increase in progression-free survival).<sup>5</sup>

Roche and Genentech are pursuing a comprehensive clinical programme investigating the use of Avastin in advanced colorectal cancer with other chemotherapies and also expanding into the adjuvant setting (post operation). As its mechanism may be relevant in a number of malignant tumours, Roche and Genentech are also investigating the potential clinical benefit of Avastin in pancreatic cancer, ovarian cancer, renal cell carcinoma and others. Approximately 15,000 patients are expected to be enrolled into clinical trials over the next years worldwide.

#### **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 a supplier of innovative

products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2004 sales by the Pharmaceuticals Division totalled 21.7 billion Swiss francs, while the Diagnostics Division posted sales of 7.8 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai.

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Roche in Oncology: [www.roche.com/pages/downloads/company/pdf/mhoncology05e.pdf](http://www.roche.com/pages/downloads/company/pdf/mhoncology05e.pdf)

**Media Relations Contacts**

Phone: +41 61 688 88 88 / e-mail: [basel.mediaoffice@roche.com](mailto:basel.mediaoffice@roche.com)

- Baschi Dürr
- Alexander Klausner
- Daniel Piller (Head Roche Group Media Office)
- Katja Prowald (Head Science Communications)
- Martina Rupp

**Note for editors**

\* In the US, Avastin is approved for use in combination with intravenous 5-fluorouracil-based chemotherapy, for first-line treatment of patients with metastatic carcinoma of the colon or rectum.

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3. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus Irinotecan, Fluorouracil, and Leucovorin for Metastatic Colorectal Cancer. *New England Journal of Medicine* 2004; 350(23): 2335-2342.
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