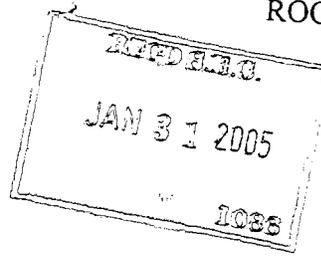


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Friday, January



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Avastin extends survival in patients with advanced colorectal cancer; new data supports its combination with widely prescribed chemotherapy
Study adds to the body of evidence showing the benefits of Avastin with different colorectal cancer treatment regimens

A new study, presented for the first time yesterday, shows Avastin (bevacizumab, rhuMAb-VEGF) significantly increases survival in patients with advanced colorectal cancer when used in combination with an oxaliplatin-containing chemotherapy regimen. This is the first phase III study to evaluate the use of Avastin with oxaliplatin and it is of particular significance as oxaliplatin-containing chemotherapy regimens are widely used in first- and second-line metastatic colorectal cancer therapy. The data were presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium, Florida, USA.(1)

Combining Avastin, an innovative new anti-angiogenesis drug, with an oxaliplatin-containing chemotherapy regimen (FOLFOX4) resulted in a significant increase in overall survival, from 10.7 months to 12.5 months, in patients with advanced colorectal cancer who had previously failed one chemotherapy regimen for their advanced disease. Data also showed that patients receiving Avastin plus chemotherapy had a 26 per cent reduction in the risk of death compared to those treated with chemotherapy alone.(1) The study (E3200) was sponsored by the National Cancer Institute and conducted by researchers led by the Eastern Cooperative Oncology Group (ECOG).

"These compelling results support the hypothesis that Avastin can prolong survival of colorectal cancer patients, independent of the type of chemotherapy that is administered. This is the third chemotherapy regimen where the addition of Avastin has shown a major benefit," commented Dr. Bruce J. Giantonio, lead study investigator, Abramson Cancer Center, University of Pennsylvania.

These results add to the growing body of evidence showing the benefit patients with advanced colorectal cancer receive when they are treated with Avastin. In a landmark study published in 2004 in the New England Journal of Medicine, Avastin showed a significant survival benefit when used in combination with chemotherapy in patients who had not received previous chemotherapy for their advanced colorectal cancer. In addition, another study showed Avastin plus chemotherapy in patients with advanced colorectal cancer showed a significant increase in progression-free survival. This study used a milder form of chemotherapy than the pivotal study, as this patient group were unfit to receive more toxic chemotherapeutic regimens.

A preliminary analysis of a second study with Avastin known as the TREE 2 trial was also presented at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium. The study evaluated Avastin use in combination with three different oxaliplatin-containing chemotherapy regimens in patients with previously untreated advanced colorectal cancer. The study showed that the addition of Avastin was well tolerated and significantly improved overall response rates when added to each of the oxaliplatin-containing chemotherapy regimens.(2)

Colorectal cancer is the third most commonly reported cancer with 945,000 new cases worldwide each year.(3)

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Avastin received fast-track approval by the US Food and Drug Administration (FDA) and was launched in the US in February 2004. In January 2005, the European Commission approved Avastin for the 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.

About the E3200 Study

Results from a preliminary analysis demonstrated that patients receiving Avastin plus FOLFOX4 had a 26 percent reduction in the risk of death, a hazard ratio of 0.74, compared to patients who received FOLFOX4 alone. Median survival for patients receiving Avastin plus FOLFOX4 was 12.5 months, compared to 10.7 months for those receiving FOLFOX4 alone, a 17 percent improvement.

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).

Results from the pivotal Phase III study published in the New England Journal of Medicine in 2004, demonstrated significantly longer survival in patients with previously untreated advanced colorectal cancer. The study, in which more than 900 patients participated, showed that Avastin plus chemotherapy increased overall survival by nearly five months (20.3 months vs 15.6 months) compared to chemotherapy alone.(4)

Roche in Oncology

Within the last five years the Roche Group, including its members Genentech in the United States and Chugai in Japan, has become the world's leading provider of anti-cancer treatments, supportive care products and diagnostics. Its oncology business includes an unprecedented five products with survival benefit in different major tumour indications: Xeloda and Herceptin in advanced stage breast cancer, MabThera in non-Hodgkin's lymphoma, Avastin in colorectal carcinoma and Tarceva in non-small cell lung cancer and pancreatic carcinoma.

In the United States Herceptin, MabThera, Avastin and Tarceva are marketed either by Genentech alone or together with its partners Biogen Idec Inc. (MabThera) and OSI (Tarceva). Outside of the United States, Roche and its Japanese partner Chugai are responsible for the marketing of these medicines.

The Roche oncology portfolio also includes NeoRecormon (anaemia in various cancer settings), Bondronat (prevention of skeletal events in breast cancer and bone metastases patients, hypercalcaemia of malignancy), Kytril (chemotherapy and radiotherapy-induced nausea and vomiting) and Roferon-A (hairy cell and chronic myeloid leukaemia, Kaposi's sarcoma, malignant melanoma, renal cell carcinoma). CERA is the most recent demonstration of Roche's commitment to anaemia management. The Roche Group's cancer medicines generated sales of more than 5.6 billion Swiss francs in the first nine months of 2004.

In addition to the medicines, Roche is developing new diagnostic tests that will have a significant impact on disease management for cancer patients in the future. With a broad portfolio of tumour markers for prostate, colorectal, liver, ovarian, breast, stomach, pancreas and lung cancer, as well as a range of molecular oncology tests, Roche will continue to be the leader in providing cancer-focused treatments and diagnostics.

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About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-intensive healthcare groups. Its core businesses are pharmaceuticals and diagnostics. As a supplier of innovative products and services for the 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 2003, the Pharmaceuticals Division generated 19.8 billion Swiss francs in prescription drug sales, while the Diagnostics Division posted sales of 7.4 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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Investor Update

Friday, January 28, 2005 8:32 AM

Breakthrough drug Tarceva provides new hope for patients with advanced pancreatic cancer New data shows significant improvement in overall survival when Tarceva is added to chemotherapy

New data, presented for the first time yesterday, have shown that adding Tarceva (erlotinib) to chemotherapy improves survival in patients with locally advanced or metastatic pancreatic cancer.(1) This is the second cancer type in which Tarceva has demonstrated a clear survival benefit and it makes Tarceva the first and only EGFR-targeted treatment to have shown a significant survival benefit in patients with pancreatic cancer and in patients with non-small cell lung cancer (NSCLC).(2) The data was presented at the American Society of Clinical Oncology (ASCO), Gastrointestinal Cancers Symposium, Hollywood, Florida.

"To have a new compound to treat this dreadful disease also offers us opportunities to strive for further improvement of treatment outcome with novel combinations," said Dr. Malcolm Moore, Study Chair and Medical Oncologist at Princess Margaret Hospital in Toronto. "This was desperately needed after so many years of frustrating attempts at finding new treatments. Tarceva opens a new era of clinical research in pancreatic cancer treatment," he added.

There was a statistically significant increase (23.5%) in overall survival in patients with locally advanced or metastatic pancreatic cancer who received Tarceva plus gemcitabine, compared to patients receiving gemcitabine alone ($p=0.025$). A higher percentage of patients were alive at 12 months in the group treated with Tarceva plus gemcitabine, compared to those treated with chemotherapy alone (24% v 17%). Progression-free survival was also significantly improved for patients treated with Tarceva ($p=0.003$).

Pancreatic cancer is the fourth leading cause of all cancer deaths; in Europe each year 60,000 people are diagnosed with pancreatic cancer and current treatment options are limited.

The multi-centre, randomised, double-blind, placebo-controlled Phase III international study was conducted by the National Cancer Institute of Canada, Clinical Trials Group at Queens University (NCIC CTG) in collaboration with OSI Pharmaceuticals. The study evaluated Tarceva at 100mg/day or 150mg/day in patients with locally advanced or metastatic pancreatic cancer. Patients received either gemcitabine with Tarceva or gemcitabine plus placebo. A total of 569 patients were randomised into the study, with 521 patients receiving 100mg/day Tarceva or placebo and 48 patients receiving 150mg/day Tarceva or placebo.

Tarceva was recently awarded FDA approval in the United States for the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen. Tarceva is also currently under review for marketing authorisation with the European and other health authorities. Early-stage trials of Tarceva are being conducted in other solid tumours, such as ovarian, colorectal, head and neck, renal cell carcinoma, glioma and gastrointestinal cancers.

About the Study

The study data demonstrated an improvement in overall survival for patients receiving Tarceva plus gemcitabine compared to patients receiving gemcitabine plus placebo (hazard ratio = 0.81, p-value = 0.025; a hazard ratio of less than one indicates a decreased risk of death and a p-value of less than 0.05 indicates statistical significance). Twenty-four percent of patients receiving Tarceva plus gemcitabine were alive after one year compared to 17 percent of patients receiving gemcitabine plus placebo. Median survival in the Tarceva plus gemcitabine arm was 6.4 months compared to 5.9 months in the gemcitabine plus placebo arm. An exploratory analysis of survival by pre-treatment characteristics also showed that patients with metastatic disease and patients with poor performance status derived a survival benefit. Progression-free survival in the Tarceva plus gemcitabine arm also was significantly improved (hazard ratio = 0.76, p-value = 0.003), although there was virtually no difference in tumor response (9 percent in patients receiving Tarceva plus gemcitabine versus 8 percent in the gemcitabine plus placebo arm).

The international study was a multi-center, randomized, double-blind, placebo-controlled Phase III trial evaluating Tarceva at 100 mg/day or 150 mg/day in patients with locally advanced or metastatic pancreatic cancer. The study randomized patients to receive either gemcitabine plus concurrent Tarceva or gemcitabine plus placebo. Gemcitabine was dosed at 1,000 mg/m² IV once weekly. A total of 569 patients were randomized in the study, 521 patients were randomized to receive 100 mg/day of Tarceva plus gemcitabine or gemcitabine plus placebo, and 48 patients received 150 mg/day of Tarceva plus gemcitabine or gemcitabine plus placebo. Approximately 75 percent of the patients in the study had metastatic disease and 25 percent had locally advanced disease. The study had sites in the United States, Asia, Canada, Europe, Australia and South America. The study was conducted by the National Cancer Institute of Canada Clinical Trials Group based at Queen's University, Ontario in collaboration with OSI Pharmaceuticals.

About Tarceva

Tarceva is an investigational small molecule that targets the human epidermal growth factor receptor (HER1) pathway. HER1, also known as EGFR, is a key component of this signalling pathway, which plays a role in the formation and growth of numerous cancers. Tarceva blocks tumour cell growth by inhibiting the tyrosine kinase activity of the HER1 signalling pathway inside the cell.

Tarceva is currently being evaluated in an extensive clinical development programme by a global alliance among OSI Pharmaceuticals, Genentech, and Roche. Chugai is pursuing its development and regulatory approval for the Japanese market.

About Pancreatic Cancer

The pancreas is a large organ lying behind the stomach that is essential in the metabolism of sugar and fat. Cancer of the pancreas strikes about 5 out of every 100,000 people and is one of the deadliest forms of cancer. Approximately 60,000 new cases of pancreatic cancer are diagnosed per year in Europe and 30,000 new cases in the US. The prognosis is poor for pancreatic cancer patients, with most studies showing 5-year survival of less than 5%. Those at the highest risk are in their 60s to 80s. Most pancreatic tumours originate in the cells of the pancreas that produce digestive enzymes (acinar cells). These adenocarcinomas account for almost 95% of pancreatic tumours.

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