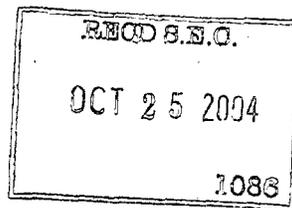




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Investor Update

Thursday, October 21, 2004 8:02 AM

Rheumatoid arthritis patients gain sustained relief from debilitating symptoms following single, short course of MabThera

Evidence supporting MabThera as an effective treatment for rheumatoid arthritis (RA) was strengthened today with the announcement that MabThera has a significant and sustained impact on the debilitating symptoms of RA following a single, short course of two infusions - just two 1g doses, two weeks apart. The data were presented today at the annual scientific meeting of the American College of Rheumatology (ACR).

In the study, 13% of patients taking MabThera, in combination with methotrexate, achieved a "Major Clinical Response" (70% reduction of RA symptoms maintained for at least 6 months) compared to none in the control group. Furthermore, the investigators found that many patients continued to derive benefit from MabThera two years after the single treatment course.

Commenting on the data, Professor Paul Emery, Leeds General Infirmary, UK, one of the trial's key investigators, said, "Not only does MabThera have a significant impact on the symptoms of RA, but it provides the longest duration of response compared to any other RA treatment following a single, short course of two infusions. These results are extremely interesting and may bring us one step closer to the goal of finding an effective and well-tolerated therapy which will offer patients with rheumatoid arthritis long-term benefit."

About the study

The multicentre, randomized, double-blind, controlled study included 161 patients from 11 countries with severe, active, long-standing RA (mean duration 10.4 years) who had not responded or responded inadequately to multiple other therapies. Patients were randomized into one of four treatment groups. The first group continued receiving methotrexate (MTX) alone (10 mg weekly), the second group received MabThera alone (2 infusions of 1g two weeks apart), the third group received MabThera (2 infusions of 1g) in combination with cyclophosphamide (2 infusions of 750 mg) and the fourth group received MabThera (2 infusions of 1g) in combination with MTX (10 mg weekly). Each group also received a 17-day course of corticosteroids (total dose of 910 mg). MabThera was infused intravenously on days 1 and 15 of the study - no further treatment with MabThera was given during the 2 years. The patients were assessed using the American College of Rheumatology (ACR) criteria and remained blinded throughout the 2 year period.

About MabThera

Unlike current RA treatments, MabThera is a therapeutic monoclonal antibody that selectively targets B cells, which are believed to play a key role in the inflammatory cascade of the disease. By doing so, MabThera aims to break the inflammatory cascade of RA - a series of reactions inflaming the synovia and leading to the cartilage loss and bone erosion that is characteristic of the disease in which B cells are thought to play a key role. MabThera has been used for over 7 years for the treatment of a form of lymphatic cancer called non-Hodgkin's lymphoma (NHL) with over 380,000 patients treated to date.

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About rheumatoid arthritis

Rheumatoid arthritis (RA) is a progressive, systemic autoimmune disease characterized by inflammation of the membrane lining in joints. This inflammation causes a loss of joint shape and function, resulting in pain, stiffness and swelling, ultimately leading to irreversible joint destruction and disability. Characteristics of RA include redness, swelling, pain, and movement limitation around joints of the hands, feet, elbows, knees and neck. In more severe cases of RA the eyes, lungs or blood vessels may be involved. RA may also shorten life expectancy by affecting major organ systems and after 10 years, less than 50% of patients can continue to work or function normally on a day to day basis. RA is one of the most common forms of autoimmune disease and affects more than 6 million people worldwide, up to 2 million of whom are in Europe.

ACR improvements

The ACR response is a standard assessment used to measure patients' responses to anti-rheumatic therapies, devised by the American College of Rheumatology (ACR). It requires a patient to have a defined percentage reduction in a number of symptoms and measures of their disease. For example, a 20 or 50 percent level of reduction (the percentage of reduction of RA symptoms) is represented as ACR20, ACR50. An ACR50 response is exceptional for existing treatments and represents a significant improvement in a patient's condition. A 'Major Clinical Response' is defined as ACR 70 maintained for at least 6 months.

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 number one in the global diagnostics market, 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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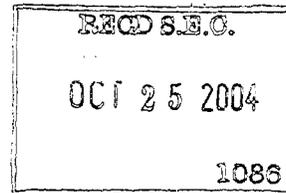
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Basel, 22 October 2004

New Genomic Method Can Identify Disease-Causing Genes with Unprecedented Precision and Speed

A novel computational method to detect disease-causing genes accurately and rapidly was announced by Roche scientists in the October 22 issue of *Science*. This approach, another innovation in computational genetic analysis from Roche scientists, promises to accelerate markedly the discovery of mouse correlates of genetic risk factors for human disease. The new approach enables researchers to identify a single causative genetic factor by correlating a pattern of observable physiological or pathological differences among selected strains of mice with a pattern of genomic variation. Using conventional methods, pin-pointing a gene contributing to disease risk could take five scientists five years. With Roche's latest innovation, which has up to 1,000-fold greater precision than current methods, a single researcher may accomplish the task in a single afternoon. The method takes advantage of the block-like patterns of genomic variation in selected mouse strains, as illustrated on the cover of *Science* in which the article appears.

"Our hope is that this new computational approach will increase the utility of the vast amount of DNA sequence information available today and help researchers more fully leverage mouse models of human disease to identify genes contributing to disease risk and drug response," said Gary Peltz, M.D., Ph.D., head of Genetics and Genomics at Roche Palo Alto. "It will help researchers understand the relationship between trait differences and variations in the mouse genome, which will move us a long way toward understanding the impact of human genetic differences. As that happens, we should be able to translate genetic data more effectively and efficiently into the development of both novel diagnostic tools and new medicines to treat human diseases."

In this regard, Roche Palo Alto is engaged in research with several leading universities and government institutions to leverage the power of the new computational technique. The studies are directed toward better understanding the genetic causes of a range of human diseases and toward pharmacogenetic analysis of how various drugs that are used commonly to treat disease work in humans.

The paper, entitled "*In Silico* Genetics: Identification of a Novel Functional Element Regulating H2-E α Gene Expression," reports that the new computational algorithm correctly identified the genetic basis for strain-specific differences in several biologically important traits, including differences in drug metabolism. The examples presented in the paper demonstrate the ability of the methodology to identify causative genetic factors accurately for a wide range of trait data. The technique also has the potential to uncover currently unknown genetic factors contributing to a host of different diseases.

Roche scientists first published a computational method for mouse genome analysis in the June 8, 2001 issue of *Science*. That method predicted regions of a mouse chromosome responsible for a trait difference. The predicted regions contained hundreds of genes and the results were assessed by relative (percentile ranking) statistical criteria. The new method offers the same analytic speed, but is much more exact, linking a single gene to a trait difference. This method eliminates the need for follow-up studies to mine large chromosomal regions, saving researchers from months to years of experimentation. In addition, the results are assessed by absolute (p-value) statistical criteria, which give researchers greater confidence in their analyses.

The pattern of genetic variation analyzed by this new computational method was created by mining a database of common genetic markers, called single nucleotide polymorphisms (SNPs), covering 1,900 genes across 16 commonly used inbred mouse strains. That database was created by Roche scientists in Palo Alto, Alameda, Calif., Basel, Switzerland, and was partially sponsored by a National Human Genome Research Institute Grant. It was recently selected as the top SNP database by respondents to a survey of scientists conducted by *Genome Technology* and *GenomeWeb Daily News*. The genetic pattern maps are now available to the public for the first time as part of the Roche SNP database web site. The web site delivers a wealth of genetic information about many mouse strains that are commonly used to model human disease.

Because the mouse genome is similar to that of humans, the mouse is the most commonly used experimental model for studying human disease, and the "mouse to man" approach is widely used. Since analyses of mouse genetic models by traditional methods are very time-consuming and

costly, this novel computational approach represents a major advance for this entire field of research.

Study participants from Roche included Guochun Liao, Jianmei Wang, Jingshu Guo, John Allard, Janet Cheng, Anh Nguyen, Gary Peltz, and Jonathan Usuka from the Roche Palo Alto campus, and Dorothee Foernzler from the Roche Center for Medical Genomics in Basel, Switzerland. Other study participants included: Steve Shafer from Stanford University, Stanford, California; Anne Peuch from the Centre National de Génotypage, France and John D. McPherson from the Washington University School of Medicine, St. Louis, Missouri.

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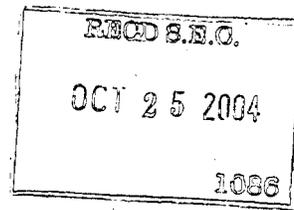
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Media Release



Basel, 22 October, 2004

Avastin receives positive opinion in Europe for the treatment of patients with metastatic colorectal cancer

Roche announced today that its innovative cancer drug, Avastin has received a positive recommendation from the European Committee for Medicinal Products for Human Use (CHMP).

The CHMP has recommended that Avastin (bevacizumab) in combination with intravenous 5-fluorouracil/folinic acid or intravenous 5-fluorouracil/folinic acid/irinotecan is indicated for first-line treatment of patients with metastatic carcinoma of the colon or rectum.

The CHMP's positive recommendation will now be proposed for final marketing approval by the European Commission. The recommendation is based on data from a pivotal Phase III study that showed that patients treated with Avastin plus chemotherapy* lived on average 30% longer than patients receiving chemotherapy alone (20.3 months versus 15.6 months)¹. Also, on average the addition of Avastin increased by 71% the amount of time that patients were without disease progression, compared to patients receiving chemotherapy alone.

"This is very good news for clinicians and patients alike," said William M Burns, Head of Roche Pharmaceuticals Division. "The CHMP's positive recommendation represents an important milestone for Avastin, as it recognises the value that Avastin can add to another current chemotherapy treatment regimen, in addition to the regimen used in the pivotal trial. It also confirms the real benefit that it can offer to patients with advanced colorectal cancer."

* Bolus 5-FU/Leucovorin/irinotecan (also known as the Saltz regimen)

Roche, together with Genentech, presently pursues 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 Avastin's mechanism may be relevant in a number of malignant tumours, Roche and Genentech are also investigating the potential clinical benefit of Avastin in other cancers, including non-small cell lung cancer, pancreatic, breast and renal cell carcinoma. Around 15,000 patients are expected to be enrolled into clinical trials over the next years worldwide.

In 2000, colorectal cancer was the third most commonly reported cancer with 945,000 new cases worldwide.² It is estimated that over 50% of people diagnosed with colorectal cancer will die of the disease.

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 interfering with the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis). It also promotes the effective delivery of chemotherapy within the tumour.

Avastin is also being explored with other chemotherapy regimens including Folfox, Xelox, Xeliri and Folfiri and Xeloda monotherapy.

Avastin was approved in February of this year in the US and has recently received full approval in Israel.

Roche in Oncology

Within the last five years the Roche Group including its partners Genentech in the US 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 four marketed products with survival benefit in different major tumour indications: Xeloda and Herceptin in advanced stage breast cancer, MabThera in non-Hodgkin's lymphoma, and Avastin in colorectal carcinoma. In the United States Herceptin, MabThera and Avastin are marketed either by Genentech alone or together with Biogen Idec Inc. (MabThera). Outside of the United States, Roche and its Japanese partner Chugai are responsible for the marketing of these drugs.

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), Kytrel (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 the commitment to anaemia management. The Roche Group's cancer medicines generated sales of more than 3.6 billion Swiss francs in the first nine months of 2004.

Roche is developing new tests, which 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, we will continue to be the leaders in providing cancer focused treatments and diagnostics.

Roche Oncology has four research sites (two in the US, Germany and Japan) and four Headquarter Development sites (two in the US, UK and Switzerland).

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For further information:

Cancer: www.health-kiosk.com

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