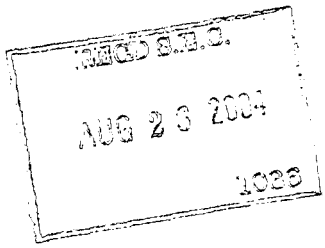
Media Release



SUPPL

Basel, 23 August 2004

New perspectives in the fight against autoimmunity

Roche researchers discover that a naturally occurring peptide influences immune response

The September issue of *Nature Immunology* reports that researchers at Roche Basel in collaboration with immunologists at the Harvard Medical School, Boston, MA have discovered a naturally occurring peptide that could play a pivotal role in the fight against autoimmune diseases. The so called CLIP (class II associated invariant chain peptide) lowers the production of those cells of the immune system that are critical in triggering pro-inflammatory immune responses, including autoimmunity. This finding may give rise to new therapeutic strategies in particular in the field of rheumatoid arthritis (RA).

"RA belongs to the group of autoimmune diseases that depend on the expansion of a subset of blood cells – so called helper T lymphocytes (T_H1)", explained Harald Kropshofer, Ph.D., Roche Head Non-clinical Immunology. "Particular T_H1 cells contribute to autoimmunity by recognizing proteins of our own body, thereby triggering adverse reactions of the immune system against the body's own tissues. At a certain stage, these T_H1 cells begin to secrete hormone-like substances, such as interferon-gamma (IFN-γ), interleukin-2 (IL-2) or interleukin-6 (IL-6), that can trigger, mediate and maintain autoimmune diseases. Hence, a peptide that helps to lower the generation rate or abundance of these T_H1 cells could be an extremely helpful approach in RA therapy".

Kropshofer's team, along with one led by Anne Vogt, Ph.D., Head Applied Immunology, Roche Center for Medical Genomics, could show in a series of preclinical studies that specialized cells of the immune system, termed 'dendritic cells', turn on the natural occurring peptide CLIP on the cell surface which reduces the number of helper T cells changing to the T_H1 type. Thus, CLIP appeared to function as a novel type of peptide regulator. More important, the researchers found that

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synthetic CLIP had the same function as naturally occurring CLIP. This opens up the possibility of using synthetic CLIP or variants thereof as therapeutic agents. CLIP mediates its activity by binding to molecules of the major histocompatibility complex (MHC) class II which are being viewed as risk factors for RA and other autoimmune diseases.

"The potential pharmacological importance of this discovery comes from the fact that modulating levels of CLIP may be used to modulate the immune response itself," said Ira Mellman, Department Head Ludwig Institute of Cancer Research, Yale University, New Haven.

About Autoimmune Diseases

Autoimmune diseases are a number of disorders, most of them serious, resulting from an inappropriate or excessive response by components of the immune system. The cause is a breakdown in the mechanisms controlling immunological tolerance to the body's own tissues. As a result, antibodies or certain T lymphocytes attack the body's own proteins or healthy cells. For Roche's immunologists, findings from basic research are the cornerstone of the quest for novel, highly specific medicines aimed as closely as possible at the root causes of autoimmune diseases and rejection reactions following organ transplantation.

A long list of clinical entities are recognised as autoimmune diseases, including multiple sclerosis, certain types of diabetes, and rheumatoid arthritis.

Based on the need for more effective treatments, Roche is currently investigating seven compounds in early stage clinical development for autoimmune diseases as well as RA.

Rheumatoid Arthritis (RA)

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 alignment, 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.

RA is one of the most common forms of autoimmune disease and affects more than 6 million people worldwide.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market and is the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of 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 employs roughly 65,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

Further information

Roche: www.roche.com
Nature: www.nature.com
Harvard Medical School: hms.harvard.edu/hms/home.asp
Yale Cancer Center: med.yale.edu/ycc/index2.htm

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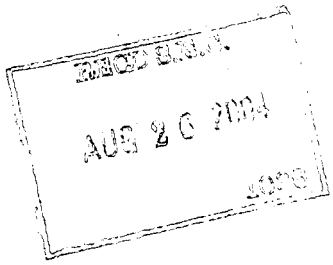

Basel, 24 August 2004

Xeloda improves therapy of patients with early colon cancer

Roche files Xeloda in Europe and the US for the treatment of colon cancer after surgery

Roche has filed an additional indication in Europe and the US for its cancer drug Xeloda to treat colon cancer patients after surgery (adjuvant therapy). Adjuvant therapy is one of the most common treatment approaches in colon cancer patients. The submission to the European and the US regulatory authorities is based on results from the successful X-ACT trial (Xeloda in Adjuvant Colon Cancer Therapy) which demonstrated that Xeloda, an oral chemotherapy treatment, could replace commonly used intravenous 5-FU/LV based therapy.

William M. Burns, Head of Roche's Pharmaceuticals Division said, "Our endeavour is to constantly improve treatment options in cancer. We are therefore pleased to be able to work with the regulatory authorities to also improve the therapy of patients with early stage colon cancer, encouraged by the outstanding results of the X-ACT study."

The global study involved almost 2,000 patients and has first been presented at this year's American Society of Clinical Oncology (ASCO) conference in New Orleans. The X-ACT trial successfully met its primary endpoint of demonstrating at least equivalent disease free survival compared to intravenous 5-FU/LV. Moreover, it proved that Xeloda reduced the risk of tumours coming back (relapse-free survival) by an impressive 14%. This means that, each year, if treated with Xeloda, nearly 4,000 additional colon cancer patients worldwide would not suffer a recurrence of their cancer.

As further presented at ASCO, Xeloda also saved medical resources compared to intravenous chemotherapy[1]. On average, a patient only needed about 8 hospital visits if treated with Xeloda compared to about 30 visits if treated with intravenous chemotherapy and Xeloda treatment

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resulted in fewer drug costs to treat chemotherapy side effects. Roche will present a full pharmacoeconomic analysis of Xeloda at this years European Society of Medical Oncology congress in Vienna, Austria.
The lead investigator Professor Jim Cassidy concluded his oral presentation at ASCO by stating: "Capecitabine (Xeloda) should replace 5-FU/LV in adjuvant treatment of colon cancer". Professor Cassidy is the Cancer Research UK Professor of Oncology and Chair of Medical Oncology, Beatson Oncology Centre, at the University of Glasgow in Scotland.

The results of the X-ACT trial further support the ongoing and planned adjuvant studies of Xeloda in combination with other chemotherapies and targeted therapy such as Avastin, enrolling over 6000 patients on a global level.

About the X-ACT study
This international, randomized, open-label efficacy and safety study evaluated 1,987 patients receiving 24 weeks of treatment with either Xeloda 1250 mg/m2, twice daily on days 1-14 of a three week cycle (n=1004), or intravenous bolus 5-FU 425 mg/m2 with intravenous leucovorin 20 mg/m2 on days 1-5, repeated every 28 days (n=983).
The primary endpoint of the study was to show that Xeloda is at least equivalent compared to 5-FU/LV in disease-free survival (DFS) which was clearly met. In a pre-planned secondary analysis, there was a strong trend detected towards superior DFS for Xeloda (p=0.0528). Moreover, relapse-free survival (RFS) was statistically superior (p=0.0407). The 3- year RFS rates were 65.5 percent for patients treated with Xeloda, compared to 61.9 percent treated with 5-FU/LV. In terms of overall survival (OS) of the two treatment groups, a trend in favour of Xeloda over 5-FU/LV was detected (p=0.0706).

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. 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), 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 the commitment to anaemia management. The Roche Group's cancer medicines generated sales of more than 3.3 billion Swiss francs in the first half of 2004.

In a recent phase III study Tarceva met its primary endpoint of improving overall survival in patients with non-small cell lung cancer. Tarceva is being developed by Roche, Genentech and OSI Pharmaceuticals. Chugai is pursuing its development and regulatory approval for the Japanese market.

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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References:
[1]Mc Kendrick et al. Capecitabine (X) is resource saving compared with i.v. bolus 5-FULV in adjuvant chemotherapy for

Dukes' C colon cancer patients: Medical resource utilization (MRU) data from a large phase III trial (X-ACT). Proc Am Soc Clin Oncol 2004;23:265 (Abstract 3578), update from poster

Further Information:

- Presentation of the X-ACT trial: http://www.asco.org/ac/1,1003,_12-002511-00_18-0026-00_19-009534-00_21-004,00.asp, "Capecitabine vs bolus 5-FU/leucovorin as adjuvant therapy for colon cancer (the X-ACT study): positive efficacy results of a phase III trial"
- About cancer: www.health-kiosk.ch

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