

Roche in Oncology – new approaches to treating cancer

- Global annual cancer incidence is set to reach 15 million by 2020
- Cancer accounts for a fifth of all deaths worldwide
- Over the past 30 years, medicinal progress has contributed substantially to significant better cancer survival rates: today, 6 out of 10 cancer patients are alive five years after diagnosis
- Oncology is a key area for the Roche Group, accounting for 25% of all research programmes and over 40% of all development projects
- Close to 45,000 patients and around 7000 centres participate in global oncology trials managed by the Roche Group
- The Group's oncology franchise includes an unprecedented five medicines with survival benefit
- Roche strongly focuses on new biomarkers of high diagnostic value and on tests for early cancer detection and risk stratification

Cancer – the global epidemic

Globally, around 11 million people are diagnosed with cancer every year. It is estimated that this will rise to 15 million by 2020. Cancer causes seven million deaths annually and is the second most common cause of death in developed countries, accounting for approximately one fifth of all deaths.

Of all new cancer cases, a third is preventable and evidence suggests that, with earlier detection using methods such as screening, a further one third of cases could be treated effectively. Whilst an increasing number of patients are being diagnosed with cancer, mortality rates are declining. Patients can now benefit from new innovative treatments that have made major improvements to outcomes.

Table 1: Changes in 5-year Survival for different cancer diseases

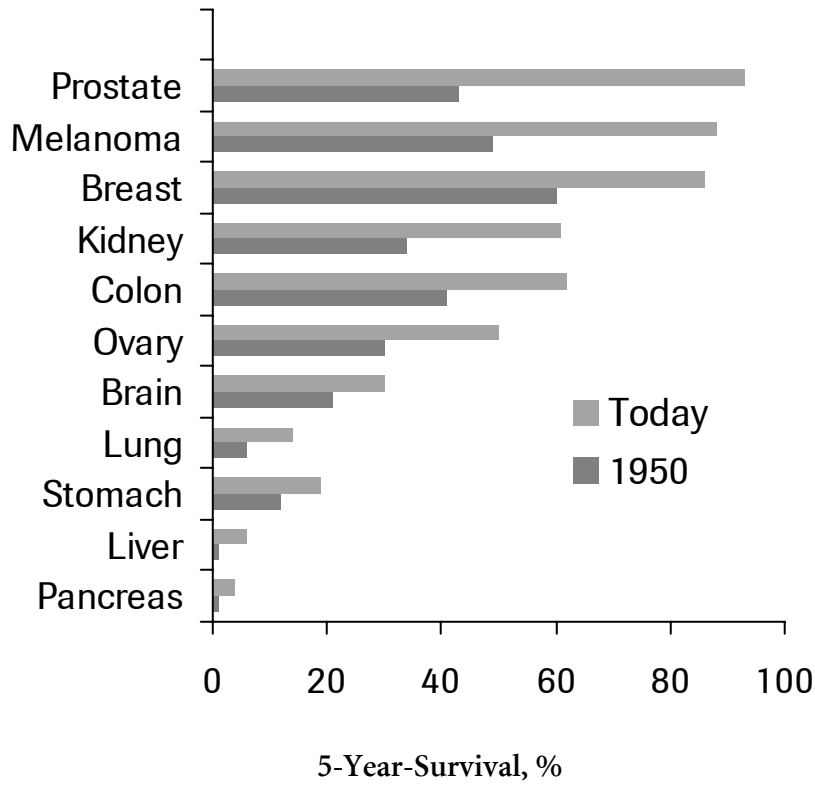
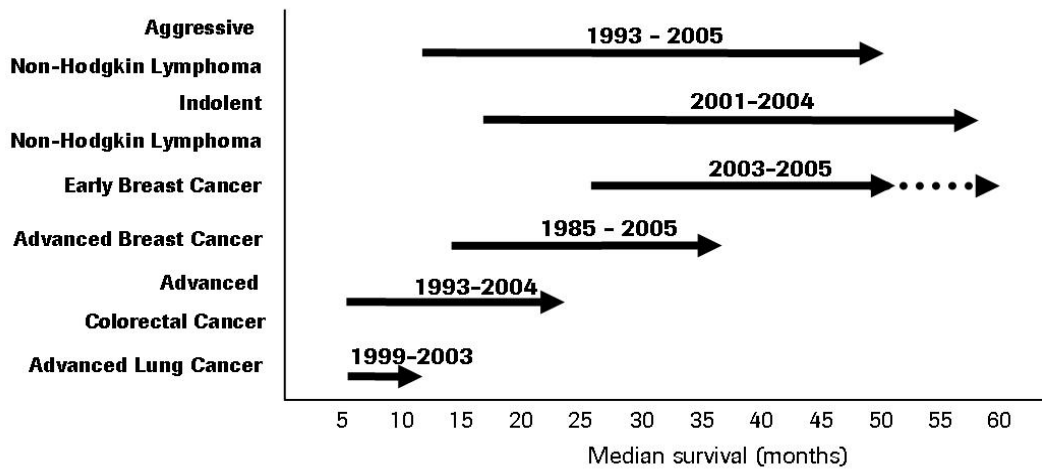


Table 2: Cancer treatment outcomes – substantial progress in recent years



Roche in Oncology – An overview

The Roche Group, including its members Genentech in the United States and Chugai in Japan, is the world's leading provider of cancer care products, including anti-cancer treatments, supportive care products and diagnostics. The Group's anticancer medicines include an unprecedented five products proven to provide survival benefit in different major tumour indications: Avastin, Herceptin, and Xeloda in advanced-stage breast cancer, Herceptin in early-stage breast cancer, MabThera in non-Hodgkin's lymphoma, Avastin and Xeloda in advanced colorectal cancer, Avastin and Tarceva in advanced non-small cell lung cancer and Tarceva and Xeloda in advanced pancreatic cancer. Roche's supportive care medicines include NeoRecormon (anaemia in various cancer settings), Bondronat (metastatic bone disease), Kytril (for chemotherapy and radiotherapy-induced nausea and vomiting) and Neupogen (for cancer-related neutropenia).

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 one of the leaders in providing cancer-focused treatments and diagnostics.

Roche's treatments against common cancers

Breast cancer

Eight to nine percent of women will develop breast cancer during their lifetime, making it one of the most common types of cancer in women. Each year more than one million new cases of breast cancer are diagnosed worldwide, with a death rate of nearly 400,000 people per year.

High levels of the HER2 protein (produced by a specific gene with cancer causing potential) are present in a particularly aggressive form of the disease called 'HER2-positive' which demands special and immediate attention because the tumors are fast-growing and there is a high likelihood of relapse. Research shows that HER2-positivity affects approximately 20-30% of women with breast cancer.

Herceptin

Herceptin is a humanised antibody, specifically designed to target and block the function of HER2. Latest data in early-stage breast cancer showed that Herceptin significantly reduces the risk of death by a third and the risk of cancer coming back by up to half. In addition, Herceptin has also demonstrated improved survival in the advanced setting, where its addition to chemotherapy

allows patients to live up to one-third longer than chemotherapy alone. Herceptin consistently benefits patients regardless of whether it is given in the early stage or advanced settings, as a single agent or in combination with chemotherapy or hormonal therapy.

Xeloda

Xeloda is an oral chemotherapy. The tablet differs from most chemotherapy because it preferentially attacks the cancer instead of healthy tissue. For patients, cancer-related pain is reduced and they do not experience hair loss. Xeloda monotherapy has shown consistently high activity in patients where other treatment options have failed. In combination with a standard chemotherapy, Xeloda demonstrated significant survival benefits.

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). It is the first and only anti-angiogenic agent to have demonstrated survival benefits in the three most common forms of cancer: colorectal cancer, non-small cell lung cancer and breast cancer. Latest data showed that Avastin plus chemotherapy doubled the time women lived with their breast cancer not progressing.

Colorectal Cancer

This is a cancer of the large bowel (colon) and back passage (rectum). In 2002, colorectal cancer was the third most commonly reported cancer with approximately one million new cases worldwide. It is estimated that over 50 percent of people diagnosed with colorectal cancer will die of the disease. In the European Union, colorectal cancer is the second most common cause of death from any cancer in both men and women.

Xeloda

Xeloda, also used for breast cancer, is the first oral chemotherapy for the treatment of patients with advanced colorectal cancer. Studies demonstrated that Xeloda achieved superior tumour shrinkage in comparison to current standard treatment. In addition, Xeloda given at an early stage (after surgery) significantly increases the number of patients free from colon cancer.

Pharmacoeconomic data also showed that on average, a patient only needed about 8 hospital visits if treated with Xeloda compared to about 30 visits if treated with intravenous chemotherapy.

Xeloda treatment resulted in fewer drug costs to treat chemotherapy side effects and is more

convenient for patients.

Avastin

Avastin, which also demonstrated clinical benefits in breast and lung cancer, showed significant survival benefits in colorectal cancer: Patients with previously untreated metastatic colorectal cancer have a 50% greater chance of being alive if treated with Avastin plus chemotherapy rather than chemotherapy alone. Additionally, other large studies investigating Avastin in combination with a wide range of chemotherapies have confirmed that Avastin enables patients with advanced colorectal cancer to live longer without progression of their disease and have also confirmed that Avastin is well tolerated.

Lung cancer

There are two main forms of lung cancer; small cell lung cancer (SCLC), and non-small cell lung cancer (NSCLC). NSCLC is the most common form, accounting for approximately 80 percent of all cases. According to WHO, lung cancer is the leading cause of cancer-related deaths in both men and women. Worldwide, there are more than 1.2 million new cases of lung and bronchial cancer diagnosed each year.

Tarceva

Currently, most lung cancer patients are treated with chemotherapy which can be very debilitating due to its toxic nature. Tarceva works differently to chemotherapy by specifically targeting tumour cells, so avoiding the unpleasant side-effects of chemotherapy. Once-daily Tarceva tablets provide a broad range of previously treated NSCLC patients significant benefits regarding survival and quality of life. In the pivotal lung cancer study, one out of three patients on Tarceva was alive at one year as opposed to only one out of five patients who had not been given the medicine.

Avastin

Avastin, which also proved to be effective in breast and colorectal cancer, showed significant survival benefits in combination with a standard chemotherapy in patients with previously untreated advanced NSCLC. In a pivotal trial, it was demonstrated for the first time that Avastin could give at least one additional year of life to advanced NSCLC patients.

Non-Hodgkin's Lymphoma

Non-Hodgkin's lymphoma (NHL) is a group of several closely related cancers that affect the lymphatic system. Of people diagnosed with NHL each year, 55% have aggressive or fast-growing NHL, which can be fatal within 6 months if left untreated. The remaining 45% of the diagnosed

suffer from indolent NHL, a slow developing form of the cancer. Patients may live many years with the disease but standard treatments cannot cure indolent NHL.

NHL is one of the fastest growing cancers; if the number of cases continues to increase at current rates, non-Hodgkin's lymphoma will have an incidence similar to that of breast, colon, lung and skin cancer by the year 2025.

MabThera

MabThera was the first monoclonal antibody for the treatment of cancer. In treating aggressive NHL, MabThera in combination with chemotherapy offers patients the best chance of a cure, compared to chemotherapy alone. This is the first time in over 20 years that a new treatment combination has been able to offer patients with aggressive NHL the chance for a longer and better life. When used as part of first-line treatment for indolent NHL (in combination with chemotherapy), MabThera prolongs life and time free from disease. Additionally, MabThera maintenance therapy for indolent NHL dramatically improves the chances of patient survival: the latest data showed that the risk of death is halved, compared to those who receive no maintenance treatment. Such a significant improvement in the outcome for indolent NHL patients has not been seen in the last 30 years.

The role of Roche Diagnostics in Oncology

Roche is stepping up its research into new biomarkers of high diagnostic value in monitoring disease progression and evaluating treatment response. Biomarkers can be used singly or in combination as sources of information. Particularly in complex diseases like cancer, tests for multiple markers are often the only means of obtaining a conclusive result. Our next generation of systems will measure marker combinations using micro arrays and protein chips.

Molecular diagnostics are also steadily gaining in importance in oncology. Roche's efforts in this area are aimed primarily at developing tests for early cancer detection, risk stratification and therapy prediction particularly for solid tumours (such as cancers of the breast, prostate and colon) A single assay format (AmpliChips) is close to development for the accurate classification of cancer diseases in hematology such as leukemia and lymphoma. Candidate markers have been identified and are currently being evaluated for potential use in these important applications.

A large-scale, international clinical research programme investigating leukemia classification is under way and due to be completed this year. There are over 20 different subtypes of leukemia, and they do not all respond to the same treatments. Choosing the most effective available

medication or type of therapy right at the outset for a particular leukemia subtype is particularly important in the acute leukemias, which progress very rapidly. A prototype test (leukemia custom chip) is expected to be ready for further research applications at the end of 2006. A similar approach is selected for the classification of lymphomas. Another micro array-based product currently in development is the AmpliChip p53 Test. Several research collaborations to investigate the potential clinical applications of this test are underway. The p53 gene is one of a family of genes called tumour suppressors, which code for proteins that prevent damaged cells from reproducing. Mutations of the p53 gene are found in virtually all tumour types. By identifying mutations that affect p53 function and activity, the AmpliChip p53 Test may one day help physicians select the anticancer medicines best suited to their patients' needs.

Glossary (non-exhaustive)

Adjuvant therapy: treatment used in addition to the main treatment. It usually refers to hormonal therapy, chemotherapy, radiation therapy, or immunotherapy added after surgery to increase the chances of curing the disease or keeping it in check.

Advanced cancer: a general term describing stages of cancer in which the disease has spread from the primary site (where it started) to other parts of the body. When the cancer has spread only to nearby areas, it is called *locally advanced*. If it has spread to distant parts of the body, it is called *metastatic*.

Curative treatment: treatment to destroy the cancer cells.

Cytotoxic: medicines that kill or damage cells.

Metastasis: the spread of cancer cells to distant areas of the body by way of the lymph system or bloodstream.

Neoadjuvant therapy: systemic therapy, such as chemotherapy or hormone therapy, given before surgery. This type of therapy can shrink some tumours, so that they are easier to remove

Palliative treatment: Palliative care is the active, total care of the patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of social, psychological and spiritual problems is paramount.

Remission: complete or partial disappearance of the signs and symptoms of cancer in response to treatment; the period during which a disease is under control. A remission may not be a cure.

Relapse: when the disease reoccurs after a remission period.

Refractory: the cancer is resistant to treatment, patient may never go into remission, possibly with stable or progressive disease.

Additional information:

About cancer: http://www.health-kiosk.ch/start_krebs