# Cancer Progress. Net

## **Major Cancer Milestones**

This timeline of advances against cancer was developed by the American Society of Clinical Oncology (ASCO), which represents nearly 30,000 physicians who treat people with cancer and research new cures. An interactive version, which includes timelines of advances against a range of common cancers, is available online at www.CancerProgress.Net.

## Overview

As a result of the nation's investment in clinical cancer research, more people are surviving cancer than ever before.

Today, two out of three people live at least five years after a cancer diagnosis, up from roughly one out of two in the 1970s. The nation's cancer death rate has dropped 18 percent since the early 1990s, reversing decades of increases.

This progress reflects advances over the last 40 years in every area of cancer care: prevention, screening, chemotherapy, surgery, radiation, and – increasingly – molecularly targeted treatments. At the same time, better ways of managing nausea, pain, and other side effects are enabling patients to live better, more fulfilling lives.

This section of CancerProgress.Net highlights some of the most important advances that have contributed to progress against cancer. From the first chemotherapy (1949) to the newest targeted treatments, nearly all of these milestones are the result of rigorously conducted clinical trials, made possible by the participation of thousands of individual patients with cancer.

#### **Timeline**

#### 1846

#### Advent of general anesthesia opens the door for modern cancer surgery

In October 1846, a Boston dentist named William T.G. Morton provides the first public demonstration of ether as a general anesthetic, allowing surgeons to remove a tumor from a patient's jaw without pain. This advance gains immediate and widespread attention, ultimately eliminating the excruciating pain experienced by surgical patients until that time, and making the modern era of surgery possible.

#### 1880s

## Radical mastectomy ushers in more aggressive surgical approaches for cancer

Baltimore surgeon William Halsted pioneers a new approach to removing breast tumors, radical mastectomy, in which the entire breast and the surrounding lymph nodes and chest muscles are removed. This helps reduce recurrences of the disease, which was previously nearly always fatal. Halsted's work also leads to similar approaches for other cancers, in which both the tumor and surrounding tissue are removed. These techniques are still an important part of treatment for some cancers today. For breast cancer, however, surgeries have become far more conservative and effective, enabling many women to avoid mastectomy altogether.





#### 1903 First use of radiation to treat cancer

Five years after Marie Curie's discovery of radium, doctors report the first successful of use of this radioactive element to treat cancer, in two Russian patients with skin cancer. In the following decades, radiation becomes widely used to treat many different cancers, including cervical, prostate, breast and other tumors. In these first decades, doctors use an approach known as brachytherapy, in which small pieces of radioactive material are implanted inside or next to tumors, delivering radiation to cancer cells at close range. Brachytherapy remains an essential part of cancer treatment today, but has been refined to more precisely target tumor cells while leaving healthy tissue unharmed.

#### 1937 National Cancer Institute established

President Franklin D. Roosevelt signs legislation establishing the National Cancer Institute to support research on the causes, diagnosis and treatment of cancer. The new agency's 1938 budget is \$400,000.

## 1943 Introduction of Pap test leads to dramatic declines in cervical cancer deaths

The Pap test, named for its inventor, George Papanicolaou, enables doctors to detect and treat cervical cancers or pre-cancers before they have a chance to spread. Since the 1950s, widespread use of the Pap test has helped to reduce U.S. cervical cancer death rates by nearly 70 percent. Yet cervical cancer remains a major cause of cancer death in developing countries, where access to screening and treatment is limited.

## 1947 First-ever remission of pediatric leukemia

Sidney Farber, a physician at Children's Hospital Boston, achieves the first partial remission of pediatric leukemia in a 4-year-old girl using the drug aminopterin. He soon documents 10 cases of remission in a landmark scientific paper. Until this time, children with acute leukemia usually died within weeks of being diagnosed. While early remissions prove temporary, they pave the way for therapies that cure thousands of patients in the decades to come, allowing most childhood cancer patients to live long, healthy lives.

#### 1949 First chemotherapy drug approved for cancer

Following results of clinical trials conducted in 1946 and 1947, nitrogen mustard is approved by the Food and Drug Administration (FDA) for the treatment of Hodgkin lymphoma. Nitrogen mustard – also known as mustard gas and stockpiled as a weapon in World War II – kills cancer cells by modifying their DNA through a process called alkylation. Its discovery spurs rapid advancements in chemotherapy, and the drug still receives some use today in combination chemotherapy for Hodgkin lymphoma.





#### 1955

## U.S. government establishes national research network to test new cancer treatments

The Clinical Trials Cooperative Group Program is established by the U.S. National Cancer Institute. Over time, this nationwide cancer research network proves the safety and efficacy of many of the most important advances in cancer treatment, screening and prevention. Cooperative Group trials have brought breakthroughs in adjuvant chemotherapy for breast and colon cancers; breast-conserving lumpectomy to avoid mastectomy; and new standards of care for blood cancers, brain tumors, and many others. Perhaps most striking is the impact of these trials on pediatric cancer survival rates. Fifty to 60 percent of children with cancer are enrolled in clinical trials, and childhood cancer survival rates have increased from less than 10 percent in the 1950s to nearly 80 percent today as a result.

## 1958 Pioneering "combination chemotherapy" cures leukemia

NCI scientists demonstrate that combination chemotherapy – in which multiple drugs are administered together – can cause remissions in both children and adults with acute leukemia. Their findings set the stage for nearly all modern chemotherapy, in which drug combinations, dosing and scheduling have been carefully refined to maximize effectiveness while minimizing side effects.

#### 1950s-1960s

## Smoking linked to cancer; cessation campaigns begin

In the 1950s, studies begin to show that smoking is a major cause of cancer, particularly lung cancer. In the early 1960s, both the U.S. Surgeon General and the U.K. Royal College of Physicians issue reports linking smoking to cancer and other serious health problems. In later years, smoking is also established as a major cause of pancreatic cancer, and second-hand smoke is declared a threat to the health of non-smokers. Tobacco control and smoking cessation soon become the most important strategies for reducing the worldwide toll of lung cancer.

## 1960 Researchers link "Philadelphia chromosome" to leukemia

Investigators in Philadelphia identify a chromosomal abnormality linked to many leukemias. A decade later, researchers discover that this abnormality results when parts of two chromosomes – chromosomes 9 and 22 – switch places in a phenomenon called translocation. It later becomes the target of one of the first-ever targeted cancer treatments, imatinib (Gleevec), which transforms treatment of chronic myelogenous leukemia and other cancers.

## 1965 Chemotherapy found to cure Hodgkin lymphoma

Researchers led by Vincent DeVita discover that a new chemotherapy regimen called MOPP (mechlorethamine, vincristine, procarbazine and prednisone) cures up to 50 percent of patients with advanced Hodgkin lymphoma. This regimen quickly becomes the standard treatment. In the 1970s, a different chemotherapy combination (doxorubicin, bleomycin, vinblastine and dacarbazine – known as ABVD) proves even more effective, curing about 70 percent of patients with advanced Hodgkin lymphoma. The ABVD combination remains a mainstay of treatment today.





#### Early 1970s

## Increased use of radioactive "seeds" to target prostate and other cancers

Studies suggest that an approach called brachytherapy extends the lives of patients with prostate cancer, compared to surgical removal of the prostate and surrounding tissue. In this approach, tiny radioactive sources or "seeds" are implanted directly into the prostate gland, delivering a high dose of radiation directly to the tumor while leaving healthy tissue beyond the prostate relatively unaffected.

Brachytherapy has been used since the early 1900s, but became less common after the widespread adoption of external beam radiation. With refined techniques and conclusive data on its effectiveness, the approach once again becomes a central part of treatment for prostate, cervical and other cancers.

## Late 1960searly 1970s

## Screening tests for colorectal cancer dramatically reduce deaths

In 1967, the guaiac fecal occult blood test (FOBT) is introduced as a screening test for colorectal cancer, one of the most common forms of cancer. This simple and inexpensive tool detects the presence of blood in stool, a sign that cancerous or precancerous growths (called polyps) may be present. Within the next few years, two new screening techniques – flexible sigmoidoscopy and colonoscopy – enable physicians to examine the colon using a small camera attached to a flexible lighted tube. The widespread use of these approaches leads to better detection of precancerous polyps and early stage cancers that are usually curable with surgery. Over the coming decades, routine screening contributes to major reductions in colorectal cancer mortality – a total decline of more than 40 percent since 1975.

#### 1971 National Cancer Act of 1971 becomes law

President Richard M. Nixon signs the National Cancer Act in December, less than a year after launching a national "War on Cancer" in his State of the Union address. The act leads to a major expansion of cancer research efforts in the U.S., paving the way for much of the progress achieved over the next 40 years. Among other changes, the Act provides unprecedented levels of funding for the National Cancer Institute (\$400 million in 1972 and \$600 million by 1974) and directs NCI to expand federal cancer research facilities and award new research grants.

#### 1971

#### More limited mastectomy proven effective for early-stage breast cancer

While radical surgery had been routinely used to treat breast cancer, a more limited surgical procedure called total mastectomy (removing just the breast tissue instead of removing the breast, chest wall muscle and underarm lymph nodes) is confirmed to be as effective for women with early-stage breast cancer. The procedure reduces pain after surgery and speeds recovery for patients. This advance paves the way for future breast-conserving surgeries.

#### 1970s

## CT scanning provides clearer images of tumors, guiding radiation and other treatments

Researchers perform the first computed tomography (CT) scan on a human patient – a woman with a suspected brain tumor. CT scanning uses X-rays to create images or "slices" of the brain, allowing doctors for the first time to clearly see tumors arising in the soft tissue of the brain. Over the following decades, CT scanning enables doctors to assess the size, shape and location of many other types of tumors, and to carefully target radiation and surgery to hit the tumors without harming healthy tissue.



## 1970s Use of cancer-causing asbestos declines

As studies confirm long-suspected links between asbestos and certain cancers, use of asbestos begins to decline. In the 1980s, its use is banned in a growing number of applications, and environmental and health regulations help to dramatically limit exposure to asbestos in workplaces and homes. Asbestos exposure has been shown to increase a person's risk of lung cancer, mesothelioma (an aggressive cancer in the chest or abdomen), and other serious health problems. Because these problems often occur decades after exposure, however, the impact of preventive efforts will be felt gradually in the years ahead

## 1975–1976 First adjuvant chemotherapy increases cure rates for early-stage breast cancer

After overcoming concerns in the cancer community about whether the benefits outweigh the risks, Drs. Bernard Fisher and Gianni Bonadonna demonstrate that chemotherapy after surgery – known as adjuvant chemotherapy – prolongs the lives of women with early stage breast cancer. Their studies involve use of the drugs I-phenylalanine mustard or a combination of cyclophosphamide (Cytoxan), methotrexate and fluorouracil. Adjuvant chemotherapy becomes a major component of treatment for the disease, improving survival and cure rates in the years ahead. Today, about 9 in ten women with early-stage breast cancer are alive five years after their diagnosis.

This finding sets the stage for research on adjuvant therapy in other common cancers, including colon and lung cancer, making it one of the most important advances in modern cancer care.

#### 1977 New treatments cure men with testicular cancer

A pivotal trial shows that combining the drugs cisplatin, vinblastine (Velban, Velsar) and bleomycin (Blenoxane) can cure 70 percent of patients with advanced testicular cancer. Cisplatin is approved by the FDA the following year. Today, the overall cure rate for testicular cancer (all stages) is a remarkable 95 percent. In recent years, the cyclist Lance Armstrong's high-profile diagnosis, treatment and recovery from the disease – and his subsequent Tour de France victories – have brought new attention to these advances, and to the vital role of clinical trials in progress against cancer.

## 1977 Many women with breast cancer can opt for breast-conserving surgery

Studies show that a procedure called lumpectomy – involving the removal of only the tumor, and not the entire breast – followed by radiation therapy is as effective as mastectomy for women with early-stage breast cancer. The finding helps dramatically reduce the physical and cosmetic side effects of breast cancer treatment and enables women to recover more quickly after surgery and return to their normal lives.

## Late 1970s Growing use of mammography saves lives

Regular breast cancer screening with mammography becomes increasingly common, helping to detect cancers at an earlier, more treatable stage. By the mid-1980s, nearly one-third of U.S. women over age 40 are screened. By 2008, the proportion screened approaches 70 percent. High screening rates – and resulting early detection – have contributed to a 27 percent reduction in breast cancer mortality among U.S. women since 1975.





## 1981 First cancer vaccine prevents cancer-causing hepatitis B infection

The FDA approves the first vaccine against hepatitis B, one of the primary causes of liver cancer. In 1991, the U.S. begins routine vaccination of all children against hepatitis B, and by 2007, the number of acute hepatitis B cases among children under 15 years declines by 98 percent. Over time, routine vaccination is expected to reduce rates of liver cancer in the U.S. and globally among adults who were vaccinated as children.

## 1982 Limited surgery helps rectal cancer patients avoid colostomies

A new procedure called total mesorectal excision emerges as a new standard surgical treatment for many patients with rectal cancer. The procedure involves removing only the cancerous region of the rectum, allowing patients to maintain normal bowel function. Previously, nearly all patients with rectal cancer had to undergo permanent colostomies (elimination of waste through an opening in the abdomen connected to a colostomy bag).

## 1986 PSA test enables early detection of prostate cancer

The FDA approves the first PSA (prostate-specific antigen) test to screen for prostate cancer – the most common form of cancer in men – in men aged 50 and older. In the years that follow, widespread use of PSA testing leads to a significant jump in early-stage prostate cancer diagnoses, sparking debate about whether such screening improves survival or simply leads to diagnosis and unnecessary treatment of slow-growing cancers that would never have become life-threatening.

## 1986 Second-hand smoke formally declared a carcinogen

The U.S. Surgeon General, and later the International Agency for Research on Cancer, officially state that second-hand smoke is a carcinogen. A number of cities around the world ban indoor smoking in the years that follow.

#### 1986 Tamoxifen reduces breast cancer recurrence

Tamoxifen (Novaldex) is approved as adjuvant therapy for post-menopausal women following breast cancer surgery, based on studies showing that use of the hormonal therapy for five years after surgery reduces the risk of cancer recurrence and dramatically increases survival.

## 1986 Global guidelines help ensure proper pain management

Pain is common among patients with advanced cancer but hasn't always been well-managed. In 1986, the World Health Organization issues clear guidance on the use of pain medications for cancer patients, focusing on stronger, opioid-type drugs such as morphine. The guidelines address widespread concerns about addiction, tolerance and abuse, which made some providers reluctant to prescribe the drugs. Adherence to the guidelines has been found to provide reliable pain relief for up to 90 percent of patients. In later years, other organizations, including ASCO, propose guidelines to help doctors recognize and talk to their patients about pain and its management.





## 1985–1991 Adjuvant therapy proven for colorectal cancer

Pivotal clinical trials show that chemotherapy following surgery (adjuvant treatment) in patients with stage III colorectal cancer reduces the risk of cancer recurrence by about 40 percent. Later refinements – using newer drugs, radiation and sophisticated treatment schedules – help to lower recurrence rates even further. Together with greater screening to detect colon cancer early, adjuvant therapy has contributed to a 40 percent reduction in colon cancer mortality in the U.S. since the 1970s.

#### Late 1980s Benzene discovered to cause blood cancers

Scientists find that occupational exposure to benzene, a chemical commonly used as a solvent and in oil-related products, is associated with increased risk of developing non-lymphocytic leukemia, non-Hodgkin lymphoma, and other diseases. Following this discovery, workers begin taking steps to protect themselves from benzene exposure and reduce their cancer risk.

## 1989 Drugs to boost blood cells help patients finish cancer treatment, reduce infections

The FDA approves the drug epoetin alpha (Procrit, Epogen) to stimulate production of red blood cells in patients with severe anemia, one of the most common and serious side effects of chemotherapy. These drugs are soon joined by white blood cell-boosting drugs such as filgrastim (Neupogen) and pegfilgrastim (Neulasta). The new treatments help reduce the need for blood transfusions and make chemotherapy safer by reducing the risk of infections and related hospitalizations.

## Early 1990s Laparoscopic surgery minimizes pain, recovery time for several cancers

Beginning in the 1990s, laparoscopic surgery – in which a surgeon makes several small incisions and uses telescoping equipment to remove tumors – emerges as an alternative to traditional open surgery for some cancers, including kidney, prostate and colorectal cancer. This new approach allows patients to recover faster and experience less pain, without sacrificing effectiveness.

## Early 1990s Shift to 3-D radiation treatment plans increases precision, safety of therapy

Thanks to the integration of powerful computers into medicine, doctors are able to dramatically improve radiation therapy by creating 3-D treatment plans. These plans require highly complex calculations and vastly more computing power than earlier, two-dimensional treatment plans. Thanks to this advance, radiation can be targeted at tumors from multiple angles, with beams of varying power, in ways that minimize the damage to healthy, surrounding tissue.

## Early 1990s Cancer deaths begin steady decline

For the first time since record-keeping began in the 1930s, cancer mortality rates begin to decline. The National Cancer Institute, the Centers for Disease Control and Prevention, and the American Cancer Society report that the overall cancer death rate fell by 2.6 percent between 1991 and 1995. Between 1991 and 2008 (the most recent year available), the death rate has fallen by a total of 18 percent.





#### 1991

## Powerful anti-nausea drugs alleviate major side effect of cancer treatment

Ondansetron (Zofran) is approved by the FDA to prevent vomiting caused by chemotherapy and/or radiation. The drug works by deactivating the nervous system's natural trigger for vomiting. Other, similar drugs are soon approved, including granisetron (Kytril), dolasetron (Anzemet) and palonosetron (Aloxi). These and other anti-nausea drugs, like aprepitant (Emend), make it possible for most cancer patients to receive chemotherapy in an outpatient setting, with minimal disruption to their daily routines.

#### 1992

## Sentinel lymph node biopsy determines cancer's spread with fewer side effects

A surgical technique called sentinel lymph node biopsy becomes a less invasive way to assess whether cancer has spread in patients with early-stage melanoma, the most aggressive form of skin cancer. The procedure involves surgically removing the lymph node closest to the primary tumor – the "sentinel" node – and examining it under a microscope for evidence of cancer. If the sentinel node is cancer-free, no further lymph nodes are removed and the patient is spared the previous practice of removing a large number of nodes. This allows for easier recovery and reduces the risk of postoperative side effects such as lymphedema, a painful swelling of the extremities.

Sentinel lymph node biopsy is later found to be effective for women with breast cancer.

#### 1970s-1990s

## Melanoma linked to sun exposure

A growing number of studies indicate that excessive sun exposure, including a history of severe sunburn, increases the risk of melanoma. However, researchers caution that some melanomas can occur in areas of the body without sun exposure, such as on the palms of the hands and soles of the feet. While researchers continue to seek a better understanding of melanoma's risk factors, a number of leading medical associations have cautioned against excessive sun exposure to reduce the risk of melanoma and other skin cancers.

#### 1992-1994

#### Taxanes emerge as a vital chemotherapy option for ovarian, breast cancer

A new family of treatments debuts with the FDA approval of paclitaxel (Taxol) for advanced ovarian cancer. The drug receives one of the fastest-ever approvals, on the heels of data showing it shrinks ovarian tumors by more than half in many women who had stopped responding to all other therapies. Later studies show it extends survival by over a year when used as an initial therapy for advanced ovarian cancer, along with the chemotherapy drug cisplatin.

Over the next decade, paclitaxel also proves effective for all stages of breast cancer – extending lives and delaying disease progression compared to existing therapies, and delaying recurrence when used as adjuvant therapy (after surgery). The drug is derived from the bark of a yew tree, and is the product of a field of research exploring 'natural' cures for a range of diseases. Until drugmakers discovered a synthetic method for producing the drug, there was widespread concern that the natural resources needed to produce the drug would not meet demand.





## 1997 FDA approves first-ever targeted cancer drug, rituximab

The FDA approves the first molecularly targeted cancer drug, rituximab (Rituxan), to treat patients with B-cell non-Hodgkin lymphoma that no longer responds to other treatments. Rituximab is in a new class of drugs called monoclonal antibodies, and targets a protein on the surface of immune cells known as B cells, interfering with the development of cancer. It is later combined with other cancer therapies to boost cure rates and increase survival.

## 1997 Surgery found to cure some patients with advanced colon cancer

In general, metastatic cancer is difficult or impossible to treat with surgery because tumor cells are spread throughout the body. But in 1997, researchers find that some colon cancer patients whose cancer has metastasized to the liver only can be cured with surgery. In a study of nearly 300 such patients who underwent surgery between 1960 and 1987, about one in four were still alive five years later, and nearly of all of these patients were found to have been essentially cured. A later study finds that use of positron emission tomography, or PET scanning, can identify some liver metastases that would have gone unnoticed before, helping surgeons in the study to achieve a cure rate above 50 percent.

## Late 1990s Prophylactic surgery helps prevent breast and ovarian cancers in women at high

In the mid-1990s, researchers discover that women who have mutations in the genes known as BRCA1 and BRCA2 have a significantly increased risk of developing breast and ovarian cancers. Soon after, studies find that women with the mutations, or with a strong family history of these cancers, may be able to reduce their cancer risk by 90 percent or more by undergoing surgical removal of their breasts (mastectomy), ovaries (oophorectomy), or both. A decade later, a major review of published studies confirms that removal of the ovaries and fallopian tubes in premenopausal women with BRCA mutations reduces the risk of breast cancer by 51 percent and the risk of ovarian and fallopian tube cancers by 79 percent.

## Late 1990s New radiotherapy technique enables precise targeting of tumors near sensitive tissue

Doctors begin using intensity modulated radiation therapy (IMRT), a highly advanced radiation technique, to precisely target tumors that lie close to vital organs and other sensitive tissue that must be protected from radiation. IMRT uses sophisticated software and complex new machinery to vary both the shape and intensity of radiation. One of the clearest benefits has been in the treatment of head and neck cancers; IMRT allows doctors to minimize radiation exposure to the spinal cord, optic nerve and salivary glands, reducing side effects without compromising tumor control.



## 1998 Drug therapy can reduce breast cancer risk in women at high risk

The FDA approves tamoxifen (Novaldex), a hormonal drug already used to prevent recurrence of breast cancer, to reduce the risk of developing breast cancer in women who are at high risk for the disease. The approval is based on a large trial showing that tamoxifen reduced breast cancer risk by more than 40 percent in women with a strong family history of breast cancer or with mutations in the BRCA1 and BRCA2 genes. Later research shows that a different drug used to treat osteoporosis, raloxifene (Evista), is as effective as tamoxifen at preventing invasive breast cancer, but with a lower risk of certain side effects.

## 1998 Treatment guidelines highlight obesity-cancer link

Major studies linking obesity to an increased risk of common cancers prompt the National Institutes of Health to publish clinical guidelines on managing obesity in adults. The guidelines point specifically to the increased risk for endometrial, breast, prostate and colon cancers, in addition to other serious health problems.

## 1998 Chemotherapy before surgery helps more women benefit from breast-conserving treatment

A major trial reports that an approach called neoadjuvant chemotherapy – providing chemotherapy before surgery – allows more than two-thirds of women with large breast tumors to undergo breast-conserving surgery, called lumpectomy, instead of full mastectomy. The goal of neoadjuvant therapy is to shrink tumors so they can be removed surgically. Breast-conserving surgery, also called lumpectomy, is easier to recover from and results in far better cosmetic outcomes – without compromising survival – compared with mastectomy. Neoadjuvant therapy is later shown to benefit patients with rectal and other cancers.

## 1998, 2006 First targeted anti-breast cancer drug, trastuzumab (Herceptin), has major impact on care

The FDA approves the groundbreaking drug trastuzumab (Herceptin) after research shows that adding the monoclonal antibody to chemotherapy dramatically increases survival for women with advanced breast cancer that over-produces a protein called HER2. In 2006, the drug is also approved as part of adjuvant therapy (after surgery) for women with early-stage HER2-positive breast cancer, after two major trials show that it reduces the risk of recurrence by more than 50 percent, an unprecedented result.

About 25 percent of breast cancer patients have HER2-positive disease, and prior to the introduction of trastuzumab, there were no effective treatments for these cancers, which were considered some of the most aggressive, deadly forms of the disease. Recently, trastuzumab was also FDA-approved to treat patients with stomach cancers that have a similar over-production of the HER2 protein.





## 2000 Study links household radon exposure to lung cancer

The lowa Radon Lung Cancer Study demonstrates that ongoing exposure to residential radon – a naturally-occurring radioactive gas that can emerge through basements and crawl spaces – is associated with increased risk of lung cancer. The Environmental Protection Agency now estimates that more than 20,000 lung cancer cases in the U.S. are due to long-term radon exposure in the home. Since the study, radon inspections have become a routine part of homeownership, promising to reduce the future burden of the disease.

## 2001 New targeted therapy transforms treatment for rare leukemia

The FDA approves imatinib (Gleevec) after just three months of review – the fastest approval in FDA history – based on data showing the drug halted the growth of chronic myelogenous leukemia (CML) in the majority of patients. Imatinib is the first drug proven to counteract a molecular defect on the so-called "Philadelphia chromosome," first discovered in 1960. It has since become the standard of care for this disease, and its effectiveness and easily-administered pill form enables most patients to live with CML as a manageable, chronic disease.

## 2001 Imatinib found highly effective against rare gastrointestinal tumor

Just weeks after being approved to treat chronic myelogenous leukemia, the targeted drug imatinib is shown to be effective against a rare abdominal tumor called GIST (gastrointestinal stromal tumor). Prior to imatinib, available drug treatments had little effect on GIST tumors. Imatinib works like a "circuit breaker" to block enzymes that can send faulty signals to trigger tumor cell growth. In GIST, it blocks the growth signal of a gene called c-Kit.

#### 1998–2003 Doubling of U.S. biomedical research budget expands cancer research

Beginning in 1998, President Bill Clinton and Congressional leaders enact a series of large, annual budget increases for the National Institutes of Health, doubling the agency's biomedical research efforts over the next five years. The new investments accelerate the pace of cancer research in the lab and in the clinic, leading to important advances over the next decade. More recently, however, federal support for cancer research has declined in real terms, potentially slowing the pace of progress against the disease.

## 2003 Scientists decode the human genome

Scientists announce that they have successfully mapped the 3 billion DNA letters in the human genome. This marks the completion of the Human Genome Project, an unprecedented international collaboration between researchers in the U.S. in and six other countries, funded primarily by the U.S. government. Results of the 13-year effort are made freely available to scientists around the world, paving the way for research to identify the genetic defects that fuel cancer, and for new ways of screening for and treating the disease.





## 2003 Obesity pinpointed as cause of many cancer deaths

An important prospective analysis involving nearly 1 million Americans reports that obesity could account for up to 20 percent of U.S. cancer deaths. Obesity is linked to a higher risk of death from liver cancer, along with several other cancer types. The researchers also estimate that 90,000 cancer-related deaths could be prevented annually if Americans maintained a healthy weight.

As obesity becomes more prevalent, researchers project that deaths from liver cancer and other forms of the disease will rise as well.

## 2003, 2004 First targeted drugs for lung cancer attack "EGFR" receptor

The FDA approves two new targeted treatments for advanced, non-small cell lung cancer, gefitinib (Iressa) and erlotinib (Tarceva). Both drugs target the epidermal growth factor receptor (EGFR), a protein on cell surfaces that is involved in driving lung cancer growth and spread. Approval is based on data showing that erlotinib extends survival in patients with advanced lung cancer – a rare finding for any treatment – and that gefitinib delays the time before a patient's cancer progresses. Around the same time, studies show that the drugs only work for patients with specific mutations in the EGFR protein. These mutations are found most often in lung cancer patients who never smoked.

To date, the two drugs are approved only for certain patients whose cancer no longer responds to other therapies. But recent studies indicate that for people with the relevant EGFR mutations, the drugs could also be valuable first-line treatment options.

## 2004 FDA approves first "anti-angiogenic" drug, bevacizumab

Bevacizumab (Avastin) is the first of a new generation of targeted drugs, called anti-angiogenics, that attack cancer by blocking the growth of blood vessels that tumors needs to grow. First approved to treat colorectal cancer, in 2004, the drug has since become an important treatment for patients with advanced lung, ovarian and kidney cancers, and for certain brain tumors, who have few other effective options.

#### 2004, 2006 Two targeted drugs approved for advanced colon cancer

The drugs cetuximab (Erbitux) and panitumumab (Vectibix) are approved to treat colon cancer that has spread to other parts of the body (metastatic disease). These drugs attack tumors that express the epidermal growth factor receptor (EGFR) protein, which is involved in cancer cell growth. Later, a coordinated analysis of multiple studies shows that cetuximab and panitumumab are effective only in patients with the normal form of a gene known as KRAS. This discovery helps physicians ensure that the drugs are used only for patients who stand to benefit, while eliminating unnecessary treatment and costs for patients who will not.

## 2004–2005 Adjuvant therapy proven effective in lung cancer

In findings that quickly change the standard of care, clinical trials show that giving chemotherapy after surgery dramatically improves survival for patients with early-stage non-small cell lung cancer, the most common form of the disease. Previously, chemotherapy was considered to be largely ineffective for lung cancer. These study results demonstrate that adjuvant chemotherapy could have an equal or greater impact on survival in lung cancer as it does in breast or colon cancer.





#### 2005

#### U.S. launches effort to map cancer genomes

The National Cancer Institute and the National Human Genome Research Institute team up to launch The Cancer Genome Atlas project. In its initial phase, the project aims to develop a comprehensive atlas of the genomes of three common cancers – lung, ovarian, and glioblastoma, a form of brain cancer. By gaining a deeper understanding of the genetic pathways involved in the development and growth of these cancers, researchers hope to identify molecular targets that can guide development of effective new treatment.

#### 2005

#### Research sheds light on long-term health problems of cancer survivors

In the 1990s, researchers begin a major study of the long-term effects of cancer and its treatment, focusing on survivors of childhood cancer. In 2005, the Childhood Cancer Survivors Study reports that survivors' risk of long-term health problems – including heart problems, second cancers and scarring of the lungs – was five times greater than that of their healthy siblings. Similar results have been found for survivors of other cancers with high cure rates, such as testicular cancer.

The results are helping oncologists and primary care providers monitor and better manage the long-term health of the millions of cancer survivors alive today.

#### 2006

## First vaccine approved to prevent cervical cancer

The FDA approves the first vaccine to prevent infection with two high-risk strains of the human papillomavirus (HPV16 and HPV18) that are known to cause about 70 percent of all cervical cancers. The vaccine, called Gardasil, is approved for girls and young women aged 9 to 26, based on a clinical trial showing that the vaccine was safe and was 100 percent effective against these types of HPV, and those that cause genital warts, for at least four and a half years after vaccination. A second vaccine, Cervarix, is approved in 2009 to prevent infection against the cancer-causing HPV strains in young women aged 10 to 25. Gardasil is later approved to prevent additional HPV-related diseases in children and young adults aged 9 to 26, including vaginal, vulvar and anal cancers in females, and anal cancer and genital warts in males. Studies have also linked HPV infection to head and neck cancers, suggesting that the vaccine may help prevent these cancers as well.

#### 2009, 2010

#### Major studies report conflicting results about benefits of PSA testing

The proper role of PSA testing remains uncertain after large, randomized trials provide conflicting results on whether routine testing reduces deaths from prostate cancer. Initial results from two studies indicate that PSA testing has minimal, if any, effect on overall survival and leads to the over-diagnosis and treatment of slow-growing cancers that are unlikely to be life-threatening. A third study finds that PSA testing reduces the risk of prostate cancer death in some men by 40 percent. Given the conflicting evidence, leading medical societies urge men to discuss the risks and benefits of screening with their doctors.





## 2010 CT scanning reduces lung cancer deaths among heavy smokers

Results from a large clinical trial show that annual screening with low-dose spiral CT (LDCT) scans reduces the risk of lung cancer death by 20 percent, compared to annual chest X-rays, in current and former heavy smokers.

The National Lung Screening Trial, funded by the National Cancer Institute, compared LDCT scanning to standard chest X-rays in this group of people at high risk for developing lung cancer. This finding marks the first-ever lung cancer screening approach that has been shown to reduce lung cancer mortality. The debate about the appropriate use of LDCT screening for lung cancer among the general population, however, continues.

## 2010 First drug shown to improve survival for patients with advanced melanoma

In a Phase III study, the targeted drug ipilimumab (Yervoy) – which boosts a specific component of the immune system – is found to improve survival and delay disease progression in patients whose advanced melanoma progresses despite other therapies. The drug is approved for this use in early 2011.

Soon after, a second trial finds that treatment using a combination of ipilimumab and dacarbazine (a chemotherapy drug commonly used in melanoma) extends survival compared to dacarbazine treatment alone.

## 2010 Adding palliative care to standard chemotherapy improves survival for advanced lung cancer patients

A head-to-head trial shows that patients who received standard chemotherapy along with palliative care (specialized treatment to address the symptoms of cancer, but not treat the disease) immediately after their diagnosis with advanced lung cancer lived three months longer and had a higher quality of life than patients who had chemotherapy alone. Patients who received the combination approach were also less likely to undergo aggressive therapy at the end of life, such as resuscitation. The results demonstrate the potential for palliative care to no only improve quality of life, but to extend patients' lives as well.

## 2011 Record number of Americans surviving cancer – nearly 12 million

The National Cancer Institute and the Centers for Disease Control and Prevention report that the number of cancer survivors in the U.S. increased to an all-time high of 11.7 million in 2007. This represents a nearly four-fold increase since 1971 (when just 3 million survivors were alive) and a 20 percent increase in the six years since 2001. The report authors highlight major progress in early detection and treatment that has led to improved survival rates, as well as the need to address the long-term health effects of cancer, and cancer treatment, among survivors.

