

America's Longest War

Much has transpired in the 40 years since President Richard Nixon announced that finding a cure for cancer would be one of his administration's top priorities. World leaders, wars, and technologies have flared and faded; nations have changed their names and borders; and one can access nearly every corner of the world with a modem and a mouse. Yet a cure for cancer continues to elude us.

It was January 22, 1971, when Nixon stood before Congress and delivered the historic State of the Union Address in which he said, "The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease." That evening, Nixon pledged more than \$100 million toward the campaign to eradicate cancer and called for a "total national commitment."

In his speech, Nixon never uttered the phrase War on Cancer, nor did this now-iconic phrase appear in the National Cancer Act of 1971, which Nixon would sign before the year was out. Yet it was clear that battle lines were being drawn. At the signing ceremony, Nixon called the Act "the most significant action taken during this administration." He also invoked the specter of war, noting that "more people each year die of cancer in the United States than all the Americans who lost their lives in World War II."

Congress also invoked combative terminology when discussing cancer. Both bodies unanimously passed resolutions that described "the conquest of cancer [as] a national crusade to be accomplished by 1976"—a year selected not because anyone believed the deadly foe could be vanquished so quickly but because it coincided with the 200th anniversary of the Declaration of Independence.

Forty years later, cancer continues to take prisoners and rack up casualties, but does this mean that the war has been lost? Leading voices in the oncology community share their views on where we stand in the War on Cancer and where they believe we are headed.

Otis W. Brawley, MD

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Dr Brawley is a global leader in the field of health disparities research. He has advised the FDA, the National Institutes of Health, the US Surgeon General, and the Centers for Disease Control and Prevention, and served as assistant director for the National Cancer Institute.

We have had dramatic declines in mortality from a number of cancers. The risk of death from colorectal, lung, and breast cancer has declined more than 30% since the early 1990s. We should be pleased with this progress but not satisfied, as we can do better.

The future will focus on development of better ways to prevent cancer and better screening technologies. A greater emphasis is being



placed on developing predictors of the biologic behavior of cancer. It has become clear that there are some tumors that can be diagnosed today that fulfill our traditional microscopic definition of malignancy, but these cancers are not genetically programmed to

spread and cause harm. The field of genomics offers great promise for this. This is the ability to assess the genetic makeup of a tumor and determine its future biologic behavior. There will soon be a day in which we will screen and diagnose a man with prostate cancer or a woman with breast cancer and tell them that it is the kind of cancer we should watch and not the kind that we should treat.

Nicholas Vogelzang, MD

Chair and Medical Director
Developmental Therapeutics Committee
US Oncology Research
Medical Oncologist
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Dr Vogelzang has authored/coauthored several peer-reviewed articles, book chapters, and abstracts. He is a recognized expert in the fields of genitourinary malignancies and mesothelioma.

Since Nixon declared the War on Cancer, we have made incredible progress that led to greater survivorship and quality of life. In 1971, every patient with metastatic testicular cancer died except [for] 5%. Today, 95% are alive and well. The average survival rate for metastatic and node-positive bladder cancer in 1971, was 6 months, with a 10% chance of survival.

Today's patients have a survival beyond 2 years and a 50% survival rate through better imaging, surgery, chemotherapy, and supportive care. The average survival rate for metastatic kidney cancer before the war was 6 to 12 months; today, patients survive 2 to 3 years, with many living beyond 5 years with a high quality of life. Patients diagnosed with metastatic prostate cancer in 1971 survived 24 months; today, they survive 48 months. Recent phase III trials of new therapies like Provenge, cabazitaxel, and abiraterone acetate should improve survival rates for metastatic prostate cancer beyond 5 years. Globally, we see advancements in melanoma, brain tumors, and breast cancer with the PARP inhibitors and more. It's amazing how many tools we have today to help patients survive. We have palpable, visible evidence that we are winning the War on Cancer. Do we need more? You bet. Continuing research is the key.



Kathryn Kolibaba, MD

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Dr Kolibaba has been a practicing oncologist/hematologist for more than 15 years. She sees patients at the Vancouver Cancer Center and is a well-known specialist in blood cancers.

Funding of cancer research and advances in molecular biology have resulted in continuous progress in the War on Cancer. Unraveling the complexities and understanding the aberrations in cancer cells in the first 25 years of the "War" has produced a growing armamentarium of targeted therapies today.



Recognizing biologically distinct subtypes of disease has led to long-term control and/or cure of previously rapidly fatal malignancies. Herceptin and imatinib are shining stars in the crown of such progress. The key to future progress and therapeutic success will be not only identifying subpopulations of cancer types driven by particular "druggable"

pathways, but targeting cancer stem cells. Drug development will continue to be more difficult, with a need to identify relevant small patient populations to develop targeted agents. Further progress will also require the development of inexpensive, rapid tests to identify the "target of vulnerability" in each person's cancer cells, matching the right drug to the individual cancer.

Brawley: Courtesy American Cancer Society/Inc.; Cisplatin: NCI / Larry Ostby; DNA sequencing: Wiki Commons;

Cancer Timeline



Kim Thiboldeaux

President and CEO
Cancer Support Community

In addition to being a tireless advocate of improving psychosocial support for patients with cancer and their families, Ms Thiboldeaux hosts the award-winning "Frankly Speaking About Cancer" Internet talk radio show and coauthored The Total Cancer Wellness Guide.

More than 12 million cancer survivors are living in the United States today. Approximately 1.5 million more people will be diagnosed with cancer this year alone. In the coming years, with the aging of 76 million baby boomers, this number will increase dramatically. Thanks to the rapid advances in screening and treatment technologies, cancer is becoming more of a chronic condition rather than a terminal illness. We are at a point in the War on Cancer where more people are living with—and fewer are dying from—cancer than ever before. As biomedical care continues to advance, it is important to broaden the focus of cancer care to include systematically addressing the social, emotional, and financial needs of the millions of people affected by the disease. Research continues to show that psychosocial support is a critical component of complete cancer care. In fact, the 2007 IOM Report "Cancer Care for the Whole Patient" asserts that psychosocial care is as important as medical care in the face of a cancer diagnosis. The Cancer Support Community and its international affiliate network, including The

Wellness Community and Gilda's Club, are committed to addressing these growing needs by providing a comprehensive menu of personalized and essential psychosocial support services for patients and families, free of charge, to ensure that no one faces cancer alone.



Lance Armstrong

Founder, LIVESTRONG
Seven-time Tour de France Winner
Testicular Cancer Survivor

At age 25, Lance Armstrong learned he had testicular cancer that had metastasized to his brain and lungs. He beat the disease despite overwhelming odds and founded the LIVESTRONG foundation to support fellow survivors and raise funds for cancer research.

Global commitment to fight back against this disease would represent a monumental advancement in public health and an enormous benefit for the world economy. Achieving that goal will require smart investment and hard work—and it can be done. We have been making progress against cancer for decades. Death rates from cancer have dropped every year since 1991, resulting in 650,000 fewer deaths from the disease. In 2007, my home state of Texas became the first in America to overwhelmingly pass a measure devoting \$3 billion to cancer



research and prevention. Many of our leading cities and nearly half our states have passed smoke-free measures; we hope that Texas will follow suit in 2011. Our nation saw the passage of healthcare reform legislation in 2010. Though the law is not perfect, it helps even the odds for cancer survivors and their

families and puts an end to the worst of the discriminatory practices many of us face.

Success in the War on Cancer requires sustained government investment in cancer research and prevention programs, ending the scourge of tobacco, and raising the profile of noncommunicable diseases, which account for 60% of the world's deaths, yet receive less than 1% of the funding. No one person, organization, or nation can win the War on Cancer. It requires an ongoing global effort and action from every single one of us.

Ahmedin Jemal, PhD

Vice President of Surveillance Research
American Cancer Society
Adjunct Associate Professor of Epidemiology
Emory University
Atlanta, Georgia

Dr Jemal is coauthor of approximately 80 scientific articles. His research focuses on applying existing cancer control knowledge into practice and cancer disparities.

Significant progress in reducing US death rates from cancer has been made since the War on Cancer was initiated in 1971. Overall cancer death rates in 2006, compared with those in 1990-1991 (peak years), were lower by 21% in men and by 11% in women; these translate to more

than 750,000 fewer cancer deaths between the peak years and 2006. This remarkable gain in reducing the overall cancer death rates since 1990-1991 is largely attributed to reduction in tobacco use over the past 50 years; increased use of screening for cervix, female breast, and colorectal cancers; and improved treatment for many cancers. However, approximately one-fifth of US adults continue to smoke, and one-third are obese. In addition, use of recommended cancer screening services is suboptimal—especially for colorectal cancer—and access to care is limited for a substantial proportion of the US population. Progress in reducing cancer death rates could be accelerated further by increased investment to apply existing cancer prevention and control knowledge into practice and to make new discoveries in cancer prevention, early detection, and treatment.



Cancer Timeline

1978

Cisplatin approved for testicular and ovarian cancer

FDA approves tamoxifen for breast cancer



1979

Crawford identifies p53 (TP53), a tumor suppressor gene

Modified radical mastectomy becomes the new standard



1980

HTLV-1 is discovered to cause T-cell leukemia



1981

Hepatitis B vaccine becomes first approved vaccine to prevent cancer

1982

Weinberg et al isolate cancer-causing genes from cancer cells



1983

Role of dendritic cells in cancer is discovered



1984

Multiple groups discover HER2

Folkman et al find first angiogenic factor

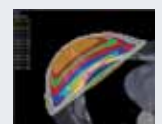
Phase I trials of Taxol begin



1985

Nerve-sparing prostatectomy is introduced

Lumpectomy/radiation combination is reported to equal mastectomy



Roy Beveridge, MD

Medical Director
US Oncology
The Woodlands, Texas

Dr Beveridge is author/coauthor of several published articles in the fields of stem cell transplantation, medical oncology, and hematology and previously served as president of the Patient Advocate Foundation.

show “All in the Family” had a scare with breast cancer, it marked the beginning of open discussions about a disease that threatened our mothers, our sisters, and our wives. Today, we as a society are much more comfortable discussing cancer, and we have raised and invested billions of dollars to fight cancer. And we are winning.

Nixon declared the War on Cancer because we had no effective therapies. Children diagnosed with leukemia in 1971 had a 70% chance of dying; today, they have a 90% chance of surviving. Through research, we have learned how cancer grows and we have developed specialized drugs, biologics, and targeted therapies that effectively kill or prevent specific cancers from growing. Today, our biggest challenge is how to afford these therapies. Specialized therapies mean more costly R&D [research and development]. We’ve come a long way, but the real question is, “Can we afford not to continue the War on Cancer?”

The War on Cancer was declared by President Richard Nixon during a time when the word *cancer* was not spoken in public; when *breast* and *cancer* were never in the same sentence and

[were] never discussed on TV. Nixon’s War on Cancer allowed the conversation to begin. When Jean Stapleton’s character Edith Bunker of the 1970’s TV



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Dr Beer’s career has focused almost exclusively on prostate cancer, and he is author and coauthor of numerous articles and abstracts on this subject.

real and substantial fruit in selected cancers. The acceleration in the accumulation of knowledge and technological capability will, however, dramatically change cancer therapy. In the near future, molecular characterization of an individual patient’s tumors to select unique combinations of targeted therapy that effectively interrupt those cancer pathways that drive that individual’s cancer will become the norm. With this paradigm shift, we expect to see a quantum leap in the effectiveness of medical therapies for cancer.

We are at the juncture of a major transformation. The investment in the human genome project and the broad and deep understanding of cancer biology has begun to yield



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Dr Hoverman is vice president of managed care for Texas Oncology and serves on the Board of Directors and Executive Council for the Austin Metro Unit of the American Cancer Society.

In 1971, post-moonwalk, pre-Watergate, [and] mired in Vietnam, President Nixon, in what became known as the War on Cancer, signed a bill that funded an “intensive campaign to cure cancer.” With a laudable goal and inspired by the space program, it was a war from which only good could come. Yet, it is a war we are still waging. There have been major scientific advances for sure, but often now, new technologies



offer progressively smaller increments of benefit at great cost, with still no cure for many

of our common cancers. Moreover, the costs of cancer are the fastest growing segment of overall costs for the healthcare system—a system at risk due to the enormity of these costs. Even with some substantial advances, we—[like] Pyrrhus—may find that it is a war we cannot afford to win.

Perhaps, as with other wars of late, this war has made us more humble. Perhaps we can address a system that delivers technology but often fails patients. Perhaps we can provide better access, screening, and prevention, giving more people cancer-free lives. And for those with cancer, perhaps we can give better care to the ones who [will] die.

Paul Bunn, MD

James Dudley Chair in Cancer Research
Professor of Medicine
University of Colorado, Denver
Aurora, Colorado

Dr Bunn’s research interests center on novel therapies for lung cancer. His studies have set standards for treating lung cancer and identified issues of natural history and biomarkers of prognosis and therapy selection.

In my mind, we are making progress in the War on Cancer, but no one fully appreciated how difficult and slow it would be. Cancer mortality rates are falling due to the improvements in early detection, prevention, and therapy that came through research and clinical trials. Some would argue that we have

made more advances in understanding basic mechanisms and in technology (eg, proteomics, genomics) than we have in translating these advances to the clinic. I believe we are now in a position to take advantage of these advances in basic science and technology. For example, in the last month we have learned that spiral CT scans used for early detection can reduce lung cancer mortality. We also learned that in advanced non-small cell lung cancer patients with an EML-4/ALK fusion, a relatively nontoxic oral pill—crizotinib—can cause regressions in about 70% of cases, and provides longer progression-free survival when compared with chemotherapy-treated historical controls. How exciting!



Retinoblastoma: NCI; mouse/DNA strand: Darryl Leja; MGR1 gene: iStock; Bone Marrow Biopsy: Chad McNeely; BRCA1 gene: Armin Kübelbeck

1986

PSA testing for prostate cancer is approved

Friend et al isolate the retinoblastoma (Rb) tumor suppressor gene



1987

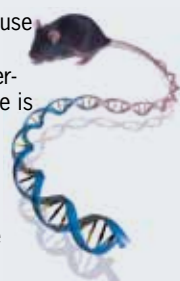
Slamon et al link HER2 to an aggressive breast cancer subtype



1988

The first mouse engineered with a cancer-causing gene is patented

Vogelstein proposes that multiple mutations cause cancer



1989

Certification in radiation oncology is first offered

VEGF gene is identified



1991

First human gene therapy is attempted in a melanoma patient



1992

FDA approves paclitaxel for use in breast cancer

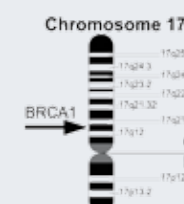
1993

Stem cell transplant is first used to treat leukemia and lymphoma



1994

BRCA1 gene is discovered



1995

BRCA2 gene is discovered

Jennifer C. Obel, MD

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Dr Obel is an expert in the treatment of breast and gastrointestinal cancers and a member of the American Society of Clinical Oncology Communications Committee.



The War on Cancer has been a comforting metaphor. It implied, above all, the existence of a single enemy that could be vanquished by a head-on attack. Nearly 40 years after declaring this War, we are wiser. We realize that each cancer has a distinct natural history that warrants a unique approach. We can now effectively cure and control certain cancers because of therapies targeted against their specific molecular pathways. Trastuzumab, an adjuvant treatment of HER2/Neu breast cancer, cures more than 30% of women with this disease. Chronic myelogenous leukemia [CML] has been reduced to a chronic

illness because of the rationally designed imatinib. These are our great victories.

However, military historians note the tendency of generals to “fight the last war”—to apply strategies that worked in the past, even as new conditions emerge. We have learned, for example, that some cancers are driven by multiple mutations: they do not have a single, salient step in their pathogenesis and, therefore, [they] defy the kinds of targeted therapies that have worked for CML and HER2/Neu breast cancer.

As we pursue *personalized medicine* to the fullest, we need to leave room for the discovery and exploration of other promising avenues of treatment. We should make sure that the useful concept of *personalized medicine* does not narrow our approach to the detriment of other promising avenues of treatment—like the War on Cancer may have done in its time.

Bernard A. Fox, PhD

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Associate Professor of Molecular Microbiology
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Dr Fox is involved in translational immunotherapy trials for patients with melanoma, prostate, ovarian, and non-small cell lung cancer, and he is president of the International Society for Biological Therapy of Cancer (iSBTc).

Significant progress is being made in the War on Cancer. Targeted therapies are providing impressive clinical benefits in select patients. With approval of the first therapeutic cancer vaccine, immunotherapy is starting to deliver on its promise to improve clinical outcomes in patients with cancer.

Nonetheless, many anticancer strategies developed from the National Institutes of Health's investment in basic science are gathering dust. The complexity of these strategies has increased and “we” have not trained, empowered, or sustained sufficient numbers of investigators to translate promising research findings into successful patient treatments. The biotech sector is cash-strapped, resulting in delays or shelving of promising agents. Public-private partnerships are at risk, and legal, regulatory, and business development concerns have limited trials of promising combination therapies. Groups, including iSBTc, are addressing [these] issues. Attention to these issues, coupled with the arrival of new vaccines, immune-potentiating agents, and immunotherapy biomarkers, will support personalized combination therapy that, over the next decade, will dramatically improve outcomes for patients with cancer.



Andrew C. von Eschenbach, MD

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Dr von Eschenbach served as director of the National Cancer Institute from 2001-2005 and commissioner of the FDA from 2006-2009.

Forty years after the National Cancer Act

committed our nation to a War on Cancer, Americans still witness far too many loved ones suffering and dying from a disease we had expected to cure. Should we admit defeat? As an oncologist, the former director of the National Cancer Institute, and a 3-time cancer survivor, my answer is *no*. This is the moment to seize victory.

Why is victory possible today when it has eluded us for decades? Forty years ago our

weapons to “seek and destroy” cancer cells were developed by trial and error. Today, after decades of research, we have begun to understand the abnormal genetic and molecular mechanisms responsible for cancer and we can now rationally design drugs and devices that “target and control” the cancer process. Even our notion of victory has changed, from expecting a universal “cure” to preventing a person's cancer from ever developing or eradicating early-stage disease or modulating the behavior of advanced disease so that patients *live with* rather than *die from* cancer. Numerous battles are being increasingly won, and the number of deaths due to cancer is declining each year. In fact, according to a recent study by the American Cancer Society, the cancer death rate has decreased by almost 2% per year for the last 10 years. We have moved from *declaring* war on cancer to now *winning* the War, and we must remain steadfast.



Cancer Timeline

Year	Event	Image
1996	The American Cancer Society releases a cancer prevention diet	
1997	The first decline in cancer deaths is reported FDA approves rituximab for non-Hodgkin's lymphoma Cancer Genome Anatomy Project is launched Cancer stem cells are discovered in acute myeloid leukemia	
1998	Herceptin approved for advanced breast cancer FDA approves tamoxifen to prevent breast cancer in high-risk women	
1999	Scientists transform a normal cell into a cancer cell FDA approves HPV screening test for cervical cancer	
2000	da Vinci robotic surgery system is approved by the FDA Diffuse large B-cell lymphoma is discovered to be 2 diseases NCI founds the Center to Reduce Cancer Health Disparities	
2001	FDA approves imatinib in chronic myeloid leukemia	
2002	Stool screening test is developed for colon cancer	
2003	Scientists develop an RNA interference technique The human genome is fully mapped Velcade, the first proteasome inhibitor, is approved in multiple myeloma	



Maurie Markman, MD

Vice President
Patient Oncology Services
National Director for Medical Oncology Cancer Treatment Centers of America
Philadelphia, Pennsylvania

Dr Markman has been involved in the research and treatment of gynecologic cancers for more than 20 years and is author/coauthor of numerous journal articles. He serves as editor-in-chief of Oncology Net Guide.

It is not unreasonable to state that we are actually at the beginning of the War on Cancer, since we now have for the first time a genuine understanding of the fundamental

molecular pathways that are the main drivers in the progression of malignant diseases. Unfortunately, we are also now very aware of the true complexity of cancer and the fact that it is highly unlikely a magic bullet will be discovered that will cure all—or most—malignant conditions. Further, evidence suggests that a more successful strategy will be to consider many advanced malignant diseases to be serious chronic illnesses, where “cure” is an unrealistic goal but where extended control (possibly measured in years) is a legitimate possibility. Importantly, a fundamental focus on control, rather than cure, has the potential to both substantially alter current anticancer drug development paradigms and increase efforts to design therapeutic strategies to maximize short-term and longer-term overall quality of life.

David J. Kerr, MD

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European Society of Medical Oncology
Rhodes Professor of Clinical Pharmacology and Cancer Therapeutics
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Professor Kerr's primary interests are treatment and research in colorectal cancer and gene therapy. He has participated in several major trials and won many distinguished awards for his professional contributions.

I think that whether it is a war or a football match, we're still in the first half of it. We often use “the battle against cancer,” or “the War” and a lot of interesting semiotics to

discuss it, and what we're doing is making small but definite gradual progress. One of my great friends, Professor Sir Richard Peto, who works with me at Oxford University and is probably the world's greatest cancer epidemiologist, has some extraordinary graphs showing the benefits we're making—particularly in breast cancer, some gastrointestinal cancers, and lung cancer. The dominant driver has not been treatment—it is the fact that through epidemiology, people are stopping smoking. Cancer survival rates are getting better, and there is some truisim in which we can definitely see the impact of chemotherapy, with improvements in breast and colorectal cancers being some of the best examples. And with these new drugs coming in, from the epidemiological point of view, we will continue to see sharp increases in cancer improvement.

Elizabeth H. Blackburn, MD

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American Association for Cancer Research
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Dr Blackburn is a 2009 Nobel Laureate in Physiology or Medicine for her contribution to the discovery of the telomerase enzyme.

We are at a point in time when cancer science and medicine have advanced dramatically, and the technologies are in place to translate breakthroughs to patients faster than ever before. People who are diagnosed with cancer today are living longer

lives and have a quality of life not previously achieved. In addition to our continued work to discover improved treatments and cures, we should focus on bringing rigorous research to bear on cancer interception and prevention. We are poised to make incredible advances in this area. By increasing our efforts to stop cancer from taking root, we can spare countless people the pain of this dreaded disease.

Marcus Neubauer, MD

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Dr Neubauer is president of the Kansas Society of Clinical Oncology. He has served as principal investigator for several clinical trials and is author/coauthor of several articles published in peer-reviewed journals.

Cancer, at least by my definition, represents unwanted growth of cells that has the capacity to spread and the potential to cause death. There are more than 100 types of cancer. So, the War on Cancer is an unfair fight. It is too hard to “cure” cancer with one fell swoop. Still, great strides have been made. Even

though some people are still dying of cancer, many are cured or, at least surviving. There are more than 10 million cancer survivors in the United States. Our focus should be steadfast to develop better treatments. Just as importantly, we need to improve prevention strategies, meet the needs of survivors, and provide compassionate supportive care to those who can't be cured. **OBTN**



2004

FDA approves Avastin, the first antiangiogenesis agent

Erbix is approved to treat colorectal cancer

2005

NCI launches the Cancer Genome Atlas Project



2006

FDA approves Gardasil vaccine to prevent HPV and cervical cancer



2007

Sorafenib becomes first drug approved for liver cancer



2008

KRAS is identified as a molecular target in colorectal cancer

Selenium is found not to prevent prostate cancer

First decline in cancer incidence is reported

2009

Multiple research groups sequence genes in breast, colon, ovarian and brain cancer



2010

Provenge becomes the first approved anticancer vaccine

Herceptin is approved for HER2-positive stomach cancer

