How knowledge becomes medical progress

New cancer drugs

vfa. Die forschenden Pharma-Unternehmen

Contents

“We are seeing revolutionary things in oncology. We are improving. And we are seeing things which we wouldn’t have dared to dream of just a short while ago.” Prof. Dirk Jäger

The vision: beating cancer

This quotation by oncologist Prof. Dirk Jäger from the National Center for Tumor Diseases Heidelberg sums up what is currently happening in cancer research.

These developments are very welcome. Most patients diagnosed with multiple myeloma in springtime in the 1990s did not live to see Christmas of the same year. Now, it is no longer rare for patients with this form of blood cancer to survive for ten years. Many—but far from all—types of cancer are on their way to becoming a chronic disease rather than a fatal one. This is not solely, but largely, thanks to new drugs: as we gain an ever better understanding of the 200+ types of cancer, the treatment options are also constantly improving. That is particularly important because many cancers are more common in later life, so an increasing number of people can expect to be diagnosed with cancer due to demographic trends.

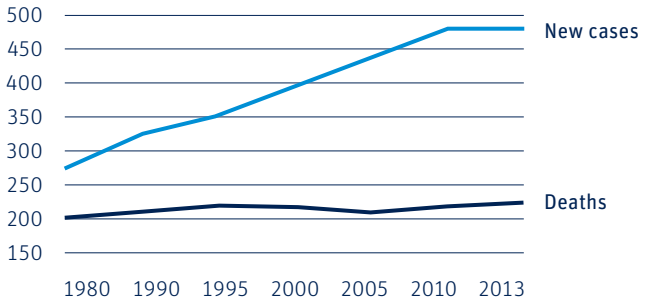
Research-based pharmaceutical companies have declared war on cancer. A third of research projects target one of the many forms of cancer because—despite all the progress that has been made—cancer is still the second most common cause of death in Germany.

We hope that this will change, which is why more than 600 molecules are now in clinical development. For research-based pharmaceutical companies, this is a challenging time. For patients, these molecules are a glimmer of hope for a longer, independent life. For a country undergoing demographic change, they represent greater sustainability.

There is even more good news: fears that spending on new cancer drugs could bankrupt the healthcare system are unfounded. Read on to find out more.

Birgit Fischer
Director General of the vfa

The number of new cases is rising, but the number of deaths is not.



Source: 2016 Report on the Incidence of Cancer in Germany, Robert Koch Institute

One of the greatest medical challenges

Cancer is as old as life itself. The disease existed in Ancient Egypt and evidence of it has even been found in dinosaur skeletons. Back then, most people died too young for cancer to be a major problem for society. However, as life expectancy increased, the focus on cancer sharpened and mankind has only been able to do anything to fight cancer for approximately the last hundred years. Even in the 21st century, cancer remains widely feared—and one of the greatest medical challenges. Why is that?

Cancer is not a single disease, but many. What is more, cancer is a complex condition. Take lung cancer, for example: Until recently, a distinction was only made between small-cell and non-small-cell lung carcinomas. Now, scientists believe there are at least two dozen variations. They place high demands on researchers because they all require different therapies.

500,000 people in Germany face a new cancer diagnosis each year—a figure which has risen by 75 percent since the 1980s due to demographic trends. Almost half of all women and men in Germany can expect to suffer from a form of cancer at some time in their life.

However, more and more people are living with a cancer diagnosis for longer. This is partly thanks to greater information, better diagnostic options enabling earlier treatment, and new, innovative drugs. It is also thanks to a boom in knowledge, due in particular to academic and industrial basic research to decipher the molecular background of diseases and a high standard of clinical research.

Cancer treatment is constantly improving. However, this does not mean we can rest on our laurels. Quite the opposite: it would be irresponsible to squander the opportunities offered by science today. We are far from reaching our goal because between 40 and 50 percent of all newly diagnosed patients still die from their cancer sooner or later.

Cancer researchers need staying power.

Skin cancer: after

30 unsuccessful years,

7 new drugs

Lung cancer:

167 failed studies,

10 new drugs

The big question: what causes cancer?

The cancer's localization is becoming less and less important. Instead, the question now is: which genetic mutations drive its growth? In the U.S.A., the first drug is already available which can be prescribed to patients with a certain genetic disposition. In this case, the genetic cause—and not the location of the tumor—is the key consideration. The trend is clear: the right therapy will increasingly be determined following a comprehensive genomic examination of the tumor, making it as tailored to the patient as possible.

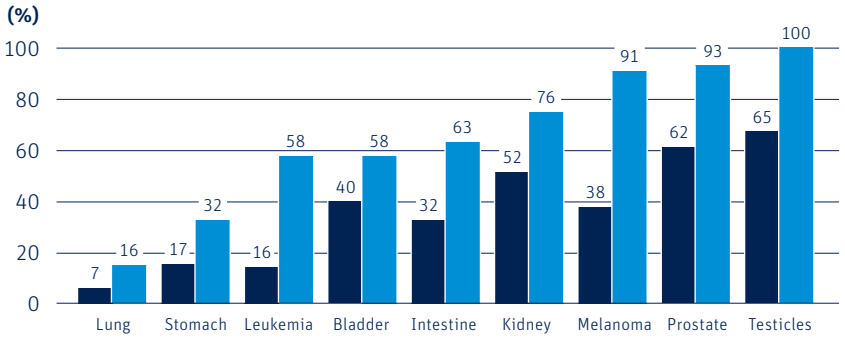
Progress in fields such as immuno-oncology has improved patients' life expectancy and quality of life. Some patients respond so well to it that they can live for many years without the disease progressing. Medics call this a "functional cure." However, immuno-oncology drugs do not help some patients at all.

This is another reason why research is ongoing. Progress has been achieved, for instance, by combining various approaches which attack the tumors in several places simultaneously, and by using antibodies as carrier molecules for cytostatic drugs to smuggle them straight into a cancer cell, slowing down the cancer cells' multiplication. Research is also being conducted into therapeutic vaccines against cancer and oncolytic viruses, which kill cancer cells by infecting them. The first few therapies using genetically modified cells are also due to be authorized in Europe soon.

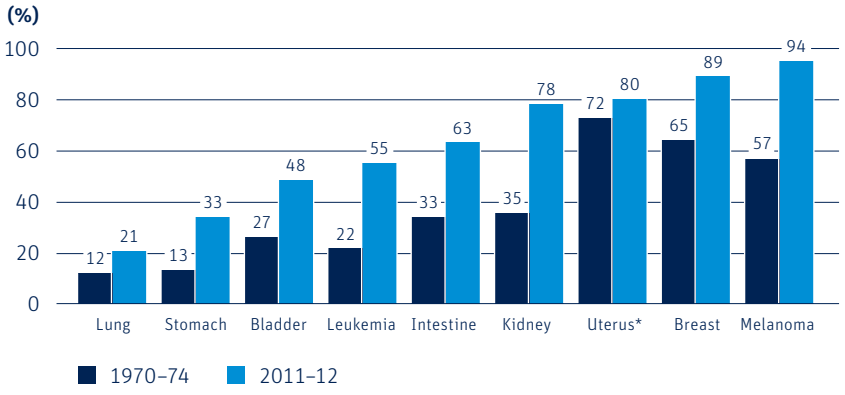
However, cancer research is complex and constantly poses new challenges: just ten new drugs were introduced for lung cancer between 1998 and 2014, for example, while 167 study programs were aborted in the same period.

Patient survival rates five years after a cancer diagnosis

Men



Women



Source: Robert Koch Institute, "Cancer in Germany, 2011/2012," 2015
* Uterine body

When will we finally have a cure for cancer?

Finally being able to declare victory over cancer is one of mankind's biggest dreams.

Mortality rates for most forms of cancer have fallen since the mid-1980s. This is thanks in large part to new cancer therapies, alongside lifestyle changes and better diagnostic and surgical options. The adjacent graph offers an overview of achievements to date: it shows patients' survival rates five years after being diagnosed with certain types of cancer. A great deal has happened—even in the case of stomach cancer, where the prognoses for patients are still poor. A man with lung cancer now has more than twice as strong a chance of surviving for at least five years after his diagnosis as in the 1970s. There are more than four million people living in Germany today who have had cancer—and almost 1.5 million of them were diagnosed more than ten years ago.

It would be irresponsible to offer an exact prediction of when we will finally be able to say that we have beaten cancer. However, we will be probably be able to cure some forms of cancer completely and keep several others in check long-term in the next 10 to 20 years. Transforming cancer into a chronic disease in this way—meaning patients would live with the condition, but without it progressing—would be a huge step forward for many cancer patients.

Up-to-date information was shared in some 6,000 talks and presentations at the world's largest cancer conference, ASCO in the U.S.A., in 2017. Every single contribution represents additional knowledge gain, and therefore another piece in the mosaic which will help us achieve our overarching goal of curing cancer.

The boom in knowledge has to be translated into concrete prospects of curing the disease. Research-based pharmaceutical and biotech companies explore disease mechanisms, find points of attack, and invent active substances to enable us to cure cancer.

Even if we cannot say when it might happen:

The vision of beating cancer is strong motivation—both for researchers at institutions and companies, and for doctors.

Variety helps: A wide range of innovative drugs is not a luxury. It is a prerequisite for the best possible cancer therapy.

The benefits of innovative cancer drugs

It will be impossible to find a single drug which cures all forms of cancer. Even within a single type of cancer, different drugs are usually needed—either one after the other or in combination with others—to keep the disease in check.

Cancer is an enemy that keeps finding new ways of growing and spreading through the body. Even if it seems to have been beaten by treatment, it often manages to evade the therapy and multiply again because a few of the tumor cells usually mutate genetically in such a way that the therapy which initially worked does not kill them. In this way, they become resistant to the cancer drug that was used, much like bacteria do to antibiotics. They then multiply to create new tumor centers, even while the other cancer cells are dying off around them.

In this situation, it is only possible to help patients if an extremely varied arsenal of drugs with different mechanisms of action is available.

That is another reason why we must not settle for the existing repertoire, but continue to develop new drugs even in areas where there is already a good range of effective medications. This is because we are seeing that new drugs can extend the lives of patients who once had poor prognoses. This extra time is thanks in part to more targeted therapies which effectively counteract the various genetic triggers. The benefits for each patient are as individual as the patients themselves.

Variety helps: A wide range of innovative drugs is not a luxury. It is a prerequisite for the best possible cancer therapy. The decision concerning the benefits of a certain drug should therefore be made by doctors and medical societies.

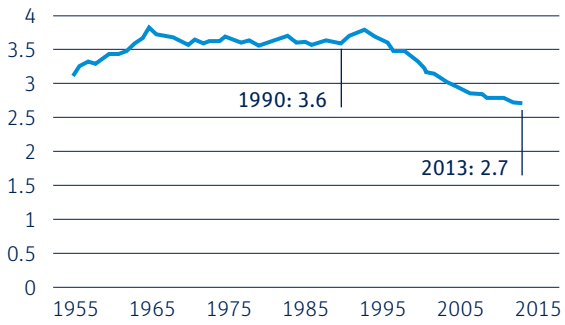
Ultimately, the objective is for the doctor and patient to be able to select the best possible therapy after weighing up the risks, side effects, and prospects of success.

There has been a

25%

reduction in cancer mortality since 1990.

Cancer deaths
per 1,000 inhabitants in Germany



Source: IGES based on figures from the Information System of the Federal Health Monitoring service, the GDR statistical yearbook, and the Federal Statistical Office; figures standardized for the extrapolated population for 2013

Three months* longer to live? That's not progress. Or is it?

When a new cancer drug is authorized, it is not the end of years of research: it is just an intermediate step. Although authorization is granted on the basis of extensive clinical studies, the study results available at this point in time only reveal part of what these drugs can do.

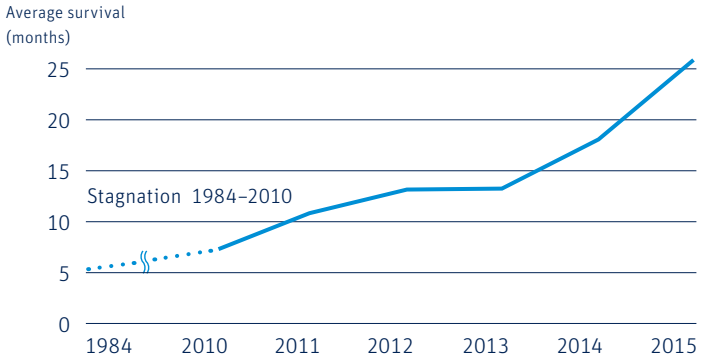
Usually, new cancer drugs are initially evaluated with patients whose condition is already at a very advanced stage and whom existing therapies can no longer help. In other words, the drugs have to prove themselves in very difficult circumstances. Only when they have shown that they can help these patients can they gradually be tested at earlier stages of the disease. This means that it sometimes takes several years to find out everything a new therapy can do. Pharmaceutical progress often takes the form of steps rather than leaps. The "three months" mentioned here by way of example (which in many cases are already substantially exceeded) are therefore an important step toward being able to transform cancer into a chronic disease or even cure it. For individual patients and their relatives, even just a few extra months can also be very precious.

This is why pharmaceutical companies keep researching even after the initial marketing authorization has been obtained. They do not just look at whether the medication is effective at earlier stages of the disease: they also explore whether it works for completely different cancer indications or in combination with cancer drugs other than those covered in earlier studies, for example.

Ultimately, it may therefore give patients years rather than months longer to live.

***The "three months" mentioned here by way of example are already substantially exceeded in many cases.**

Example: metastasized skin cancer. Survival times have more than doubled in the last ten years.



Source: Robert C et al. *Ipilimumab plus dacarbazine for previously untreated metastatic melanoma.* N Engl J Med. Jun. 30, 2011; 364 (26): 2517–26
Robert C et al. *Nivolumab in previously untreated melanoma without BRAF mutation.* N Engl J Med. Jan. 22, 2015; 372 (4): 320–30
Tas F. *Metastatic behavior in melanoma: timing, pattern, survival, and influencing factors.* J Oncol. 2012; 2012: 647684

Still pie in the sky? Perhaps, but …

Knowledge drives innovations. New findings from the basic research conducted by our member companies and from public research at universities and institutes give rise to ideas for new treatment options.

There is still a lot to do in the battle against cancer. However, a look at the not-so-distant past offers an interesting comparison: Cardiovascular conditions used to lead to a premature death in the vast majority of cases. Only after extensive research resulting in the development of effective medication—coupled with lifestyle changes—was it possible to achieve major successes. The more knowledge we have, the better the treatment options and the greater the effect on patients' health. Nowadays, many cardiovascular conditions can be treated effectively, the cost of the drugs is low, and the benefits are huge.

Will it be possible to replicate this success in the field of oncology? Here too, a great deal of research is being conducted—and progress is already being made. However, cancer treatment is complex and cancer is more heterogeneous than all the cardiovascular diseases put together. With that in mind:

We will only achieve this kind of success in cancer therapy with even more research activities and a great deal of staying power.

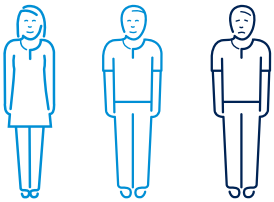
In many cases, the full benefits of innovations only become clear with time, so it often takes courage and farsightedness not to reject therapeutic alternatives too hastily. Many of today's gold-standard therapies only revealed the full extent of their effectiveness after a number of years.

The example of cardiovascular diseases also teaches us that knowledge leads to progress which may be costly at first, but soon results in high-quality, cost-effective therapy as competitors' products emerge, followed later by generic drugs.

Spending on cancer drugs
only accounts for approximately

2%

of the statutory health insurance
providers' total expenditure.



Two out of three people who have
successfully undergone cancer therapy
return to work, creating new value for
society and the economy.

Can we afford progress?

Finding therapies for the various forms of cancer is far from easy. Developing drugs which are increasingly effective, have fewer side effects, and can be used in an increasingly personalized fashion is time-consuming and financially risky.

By contrast, it is very easy to answer the question of whether the many new cancer therapies will remain affordable. All you have to do is take a look at two facts: First, €17 of each €100 that the statutory health insurance providers pay out to treat their clients goes toward drugs. Second, oncology accounts for approximately 13 percent of this spending. This means that oncology drugs only make up about 2 percent of health insurance companies' expenditure. That is €2 in every hundred to tackle the second most common cause of death in Germany.

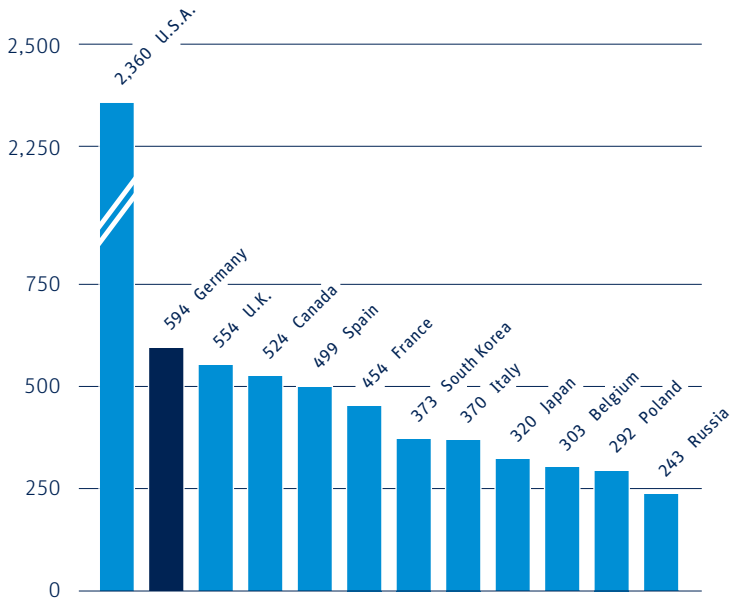
Is that too much?

It is true that the proportion of total spending which goes toward cancer drugs is only increasing modestly—despite the fact that more and more people are suffering from cancer and ever-better drugs mean that these patients are living longer and therefore taking medication for longer periods of time.

What is more, we are now able to treat patients for whom there were recently very few drugs available, such as those with malignant melanoma. A moderate rise in cancer drug spending is the logical consequence of increasingly good treatment options—and therefore essentially good news.

In Germany, pharmaceutical innovations are often accompanied by apocalyptic reporting: this was the case with HIV drugs, the first personalized breast cancer therapy, vaccines against cervical cancer, and the new hepatitis C medications. None of these pessimistic predictions came true, and it is safe to say that cancer drugs will not lead to a financial disaster either. The competition posed by other drugs—along with generic options and biosimilars once the patents have expired—also helps to bring costs down.

International comparison of the number of clinical studies by research-based pharmaceutical companies in 2016



Source: vfa based on the database of studies at ClinicalTrials.gov; correct as of October 2017

Germany: a cancer-fighting powerhouse

Germany plays a key role in the global battle against cancer: excellent research facilities, outstanding scientists, medical staff with first-rate training, world-class clinical centers, and research-based pharmaceutical and biotech companies which capitalize on the advantages offered by the country to make tomorrow's cancer therapies a success.

More than a dozen vfa member companies have their own cancer research laboratories in Germany: in Berlin, Cologne, Wuppertal, Penzberg, Munich, Ludwigshafen, Darmstadt, Mainz, and Tübingen. Cancer research is the number one focus of industrial pharmaceutical research in Germany.

Furthermore, no other country in the world—except for the U.S.A.—is home to more industry-initiated clinical studies than Germany. This primarily benefits patients in Germany directly, but that is not all: research-based pharmaceutical companies and the studies they initiate act as a motor for Germany as a hub of innovation and knowledge.

Most of these studies conducted here explore forms of cancer: a quarter of the 594 studies that commenced in Germany in 2016 were devoted to various cancers. Their value does not only lie in the fact that they contribute towards the development of new therapies. For many participants for whom existing therapies are no longer effective, these studies represent an opportunity to be treated with a new drug that might help them.

The large number of clinical studies conducted in Germany is one of the reasons why our healthcare system is among the best in the world.

Outlook: we decide today whether we will beat cancer tomorrow.

There is no doubt as to the goal: we want to beat cancer one day. There are plenty of hurdles on the way to achieving this: we do not yet have all the information we need to be able to say that cancer can be cured.

While this remains the case, research must continue undiminished. Research-based pharmaceutical and biotech companies use the ever-growing pool of knowledge concerning the fundamental principles of cancer to make a crucial contribution.

Pharmaceutical research is striving with determination to translate new scientific findings from basic research into the prospect of a cure. However, it usually takes more than ten years before an idea for a new drug is transformed into a marketing authorization. With this in mind, we decide today whether we will beat cancer tomorrow.

In the light of this, we need a healthcare system which recognizes and supports the value of innovations. Especially when it comes to cancer, new therapies are not just an investment in patients' health: they are also a healthy investment in the sustainability of our ageing society.

Health spending is an investment in the future. Especially with regard to new, ground-breaking cancer drugs, we should see this expenditure as an opportunity for individuals, for medical progress, and for society as a whole.

"The chance of beating cancer has never been as concrete as it is today. With knowledge of the fundamental principles of these diseases growing almost by the hour, we are becoming better and better at finding the right answers to what remains the greatest medical challenge. Our companies need a innovation-friendly environment to succeed because we decide today whether we will beat cancer tomorrow."

Birgit Fischer
Director General of the vfa

Ensuring that knowledge becomes medical progress means:

1. Making sure that all patients have access to the best possible cancer therapies for them

2. Further developing the healthcare system to make it reliably and open to innovation

3. Securing investments in research, development, and production in Germany

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