Prize for journalist who tackled taboo subject of rationing cancer therapies

Restricting access to cancer treatments is an emotive topic that politicians avoid when possible – nowhere more so than in Germany. **Nicola Kuhrt** won an award for her informative and sensitive article on this subject, entitled *Cancer therapy: What is a month of life worth?* which was originally published in the respected *Frankfurter Allgemeine Sonntagszeitung*, and is reprinted below.

20 January 2010. The holiday is desperately needed. On her doctor's advice, Anna Brinckmann has been on a 'drug holiday' for a week. It will give her a chance to recover from the side-effects of her treatment. Anna, who lives in Berlin, knows the ropes: she has already had several courses of chemotherapy with Erbitux. The drug is one of a whole group of new substances that many people see as representing the future of cancer therapy. Antibodies with special properties developed in the laboratory are designed to attack the disease with more precision than before.

Anna Brinckmann knew that around twenty per cent of Erbitux patients experience unwanted reactions. For her the side-effects always start with pus-filled pimples on her face. Her skin burns as though on fire. Even washing it with distilled water is painful. But she is also aware of the other side of the picture, with its optimistic message: the worse the skin rash, the more effectively the therapy is working. "Unpleasant, but true", was how the doctor explained it to her.

Anna Brinckmann has advanced colorectal cancer. Various studies have investigated how much longer colorectal cancer patients live if they take Erbitux. One reported a "statistically significant improvement" in survival from 20 to 23.5 months by comparison with conventional treatment; in another, patients treated with Erbitux lived on average 2.9 months longer. But what use are statistics in an individual case? Before each new course of treatment Anna Brinckmann must decide whether she wants to go on – with the hope of extending her life a little, but with the risk of severe side-effects – or whether the time has come to call a halt.

Nicola Kuhrt

It is not only the patients for whom the new, targeted drugs pose a dilemma. The new treatments cause the costs of cancer therapy to rocket. At a monthly cost of €4000 or more per drug, the annual cost per patient quickly mounts up to between

Frankfurter Allgemeine
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Who decides what an extra month of life is worth? This well-written and sensitive feature encourages readers to join a debate on priorities for health spending that might otherwise be conducted out of the public eye by unaccountable civil servants and medical insurance bureaucrats


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Was darf ein Monat Leben kosten?

Das Abc der Krebstherapie

€40,000 and €100,000. Surely the health system can ill afford to fund such treatments, which after all add only a few weeks to survival times?

Politicians are reluctant to address this issue. Doctors, too, hesitate to speak out. When Jörg-Dietrich Hoppe, president of the German Medical Association, forecast recently that the gap between what is medically possible and what is affordable would continue to grow, he drew criticism from all sides; the unanimous view was that his remarks were "inhumane".

But Germany will not be able to avoid the discussion of ethics and efficiency in the health service for much longer. The ageing of the population inevitably means that some therapies will at some point have to be rationed. Personalised cancer drugs could set a precedent for this.

A BOOM MARKET

Oncology is becoming the highest-turnover segment of the pharmaceutical industry. Analysts at the market intelligence company IMS Health have calculated that sales of cancer drugs by pharmaceutical companies worldwide totalled $48 billion in 2008; the figure has doubled since 2003. A further rise to $75 billion dollars is forecast by 2013.

As a result there is hardly a pharmaceutical company anywhere that is ignoring the trend and not researching at least one new cancer drug. More than 300 potential new drugs are currently in development – twice as many as for heart disease, strokes or Alzheimer's. "Innovation in medicine comes with a price tag," explains Hagen Pfundner, CEO of the leading company in the sector, Roche Pharma AG. He points out that a pharmaceutical company is a business like any other; it must pay wages and its shareholders expect to see returns. Nevertheless, Roche is investing around twenty per cent of its turnover in research, exposing itself to considerable risk in the process. "Today's innovation is tomorrow's low-cost medicine," explains Pfundner. The first drugs for tackling the AIDS virus and the early cardiovascular drugs were also very expensive, he says, but in those cases nobody talked about the price.

Cancer researchers have for years been dreaming of targeted therapies. More than a century ago the German Nobel prize winner Paul Ehrlich had the idea of preparing antibodies in the laboratory and using them to target tumours. Because of the

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complexity of the disease, his successors are still working on putting the plan into practice: the task is difficult because tumours afford too few points of attack, cancer cells are too flexible and the emergence of resistance is too common.

There is no lack of experiments. Many of the protein molecules that have now been developed inhibit the processes that would otherwise result in the constant reproduction of cancer cells. Others interrupt signal pathways that cancer cells need to survive. Genetic tests can often determine in advance whether the drug will be effective in a particular patient or not. The therapy is then not only targeted but also 'personalised'. Marketing strategies like to refer in this context to 'made-to-measure' pills. Substances that intervene in specific processes in the tumour cell are known as 'smart molecules'.

One of the antibodies of the early days was Rituximab from Roche. This laboratory-designed protein recognises a characteristic feature on the surface of cancer cells in patients with a B-cell lymphoma. The drug, which is usually used in combination with chemotherapy, appeared on the market in 1997. It is estimated that the number of people who die from B-cell lymphoma has fallen by fifty per cent in the last ten years.

Glivec has also become well known. It has significantly improved the survival prospects of patients with a particular form of leukaemia. Over the past year Glivec alone has brought in revenue of €2.6 billion for its manufacturer, Novartis.

It is the spectacular successes of this sort that make the whole field of cancer drugs so attractive for pharmaceutical companies. On the market, however, very few of the subsequent products have yielded much real benefit for patients. "The patients live at best three or four months longer than with conventional treatment. Their quality of life is not improved," says the chairman of the German Medical Association's Drug Commission, Wolf-Dieter Ludwig. Many oncologists have been disappointed by the new drugs.

Ludwig also notes that the costs of new drugs in oncology are rising much faster than the evidence of their usefulness. In many cases there are no reliable markers for testing whether or not the targeted drug is effective. For example, for monoclonal antibodies which block the epidermal growth factor, the only guideline is often the crude

£30,000 IS THE LIMIT

The cost of a drug can vary widely from country to country. In the US and Germany pharmaceutical companies are still free to set the prices of their products themselves, but in other countries the conditions under which a drug can be marketed is usually negotiated during the licensing process.

The UK National Institute for Health and Clinical Excellence (NICE) takes a particularly firm line on this issue. The health authority evaluates new therapies in terms of QALYs – quality-adjusted life-years. A QALY is an additional year of life of good quality – the threshold is currently £30,000. If a treatment, including the drug treatment of a cancer patient, costs more than this it cannot be provided free of charge through the tax-funded British health system. In the past NICE has rejected a number of cancer drugs, including Bayer's Nexavar, used for liver cancer, the lung cancer drug Tarceva from Roche and Erbitux from Merck, which is used to treat bowel cancer.

The strict price policy of the UK health authorities has met with strong criticism from politicians and patient organisations. The protests have, however, become more muted since many pharmaceutical companies have now indicated that they are prepared to reduce their prices. For example, Celgene has agreed to provide the cancer drug Revlimid free of charge from the third year of treatment. Pfizer, too, has made concessions to the UK authorities: the kidney cancer drug Sutent is now available free for the first six-week treatment cycle. In addition, NICE has come to an agreement with the Spanish company Pharma Mar, under which Pharma Mar will cover the costs of treatment with the sarcoma drug Yondelis from the fifth treatment cycle.

DIETER RÜCHEL

principle of "If pimples, then sensitive".

Wolfgang Dietrich, head of the oncology division at Roche, describes the situation elegantly: "We haven't yet discovered the tailor-made suit, but we have the one-size-fits-all version". But tailor-made drugs are not far away – drug and diagnostics research have been running in parallel for some time. "The aim of course is to put each drug on the market complete with an appropriate marker – not to have the drug first and then run studies to discover which groups of patients it is suitable for."

However, a growing number of these studies are being terminated at a very early stage – even when there are preliminary signs of success. The pharmaceutical companies justify their action on the grounds that the therapy cannot simply be withheld from the members of the control groups who, in accordance with the study protocol, receive only a placebo. But it then becomes impossible to collect data either on the long-term efficacy of the drug or on occasional side-effects.

Costs and benefits

Further criticism comes from another quarter. According to Lilli Grell of the Medical Services Department of the Association of Health Insurance Funds (MDK), cancer studies are not now concerned with how much longer a patient lives as a result of a new drug; they only consider the length of the interval between the conclusion of treatment and return of the tumour. "It is not uncommon for a drug to extend this interval. But the patients still die just as early as those treated conventionally." And it would be wrong to believe that the innovative cancer drugs are free of side-effects. The side-effects are simply different. Whereas conventional chemotherapy was frequently accompanied by diarrhoea, vomiting and hair loss, patients must now reckon with severe skin reactions, inflammation of the brain, extreme tiredness and liver damage.

It is Grell's job to cast a critical eye over pharmaceutical innovations. The Medical Services Department for which she works is called on to make a decision when it is unclear whether statutory health insurers should cover the costs of treatment. In oncology such queries arise relatively frequently, says Grell, because cancer drugs are often used outside the approved indications – either because they are still very new, or because there are studies that suggest to doctors that the drug is worth trying. In some cases, too, a particular drug is used because the patient is already so sick that no further standard therapy is available.

Many cancer doctors prefer to say "I've got something else to try" rather than articulate the uncomfortable truth, which may be "There is nothing more I can do for you." Increasingly often, though, the request comes from patients. They read about new drugs on the Internet or in magazines and are then determined to try them.

"It needs a good relationship between doctor and patient to look at such issues together," says Annika Siegmund, a doctor at the National Center for Tumour Diseases in Heidelberg. Of course it may be possible to delay the advance of the disease, and hence the patient's death, for a certain time. "But unfortunately it is impossible to know in advance whether the treatment will be successful and how severe the side-effects will be." Sometimes, she says, one must also protect patients from themselves.

"The decisions that cancer patients now have to take are tough," explains Annika Siegmund. They ask themselves questions such as: "How much can I take, so that I have a chance of seeing my grandchild start school?" Or, "Am I actually too vain to want to battle with severe skin reactions on my face during the final months of my life?"

Anna Brinckmann from Berlin has made her decision. She wants to go on. But only one more time. "Then I will really have had enough."

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