# Single-case therapy or clinical trials in disguise?

Several German clinics and physicians are under investigation for allegedly conducting clinical trials under the guise of prescribing drugs for non-approved uses. A public prosecutor has been informed by the biggest German health insurance company, AOK, that several hundred patients, most of whom have malignant melanoma, have been treated over the past ten years with the interferon-β drug Fiblaferon, which is not approved in Germany for melanoma. Fiblaferon is produced by the German drug company Rentschler and was approved by the German health authorities in 1984 only for the treatment of three life-threatening viral diseases and nasopharyngeal carcinoma.

This case is the latest incident in a long-running controversy in Germany about the question of who is going to pay for clinical development of new therapeutic substances. Under certain circumstances the use of drugs not approved for a particular indication is covered by German health-care regulations: If a patient with a life-threatening disease such as melanoma fails to respond to standard therapy, his or her doctor can treat the patient with a non-approved drug, if the option is suggested in the medical literature. In this case, interferon-β is already approved for malignant melanoma in Japan.

For reimbursement of such single-case therapies, treatment of the patient must be the doctor's only intention, not drug development, which can only be done in clinical trials. Drugs used in clinical trials must be provided free of charge by the company developing the drug. A nationwide cross-checking of reimbursement forms for Fiblaferon in melanoma patients at the AOK headquarters in Bonn revealed not only a relatively high number (about 50 patients per year) but also a pattern of certain clinics and doctors using the drug for such patients. "At least in some cases we have the impression that the treatment was induced by the company to conduct some sort of clinical trial," says Gerd Glaeske, an expert from the German association of medical insurance companies for employees. "If this is true, the doctors wrongly declared the treatment to be single-case therapy to get insurance reimbursement." Now the public prosecutor is investigating whether systematic testing of the drug took place in melanoma patients.

The bill to be paid by German insurance companies for Fiblaferon in melanoma patients is substantial. A complete two-year course of treatment for one patient can amount to US$60,000. Total yearly sales for Rentschler's Fiblaferon are $8–$10 million. Glaeske says, "Fiblaferon sales for melanoma patients make up a substantial part of that income."

Glaeske's suspicion that a clinical trial is under way is substantiated by the fact that several clinics and doctors reported patients' data to Rentschler. In return, Rentschler paid the doctors a fee of roughly $200 for five years of patient documentation, according to Rentschler spokesman Ernst-Wilhelm von Wedel.

Von Wedel calls the treatments 'an open therapeutic study', a term not defined under German health care regulations. But von Wedel denies "any financial interest of the company in these studies." He adds: "The data gathered in such open studies are not sound enough statistically to be used in the approval process." Meanwhile, Rentschler has started a clinical study to seek approval for its interferon-β in certain stages of melanoma. "The documentation within the open studies," von Wedel claims, "was only done for the sake of interpersonal quality control of the different treatment regimens." This is another name for efficacy testing.

As Glaeske puts it, "some drug companies try to penetrate the market with their drugs before getting approval — that's why they are interested in building up the 'open study category', which is somewhere in between single-case therapies and clinical trials."

Meanwhile, the small Munich-based drug company Medmark is seeking approval for its first product, the anti-cancer drug Edelfosin. Because of the high production costs Medmark argued in the Constitutional Supreme Court that it would go bankrupt if it had to provide the drug for clinical trials free of charge. The Supreme Court has temporarily lifted the legal obligation of drug companies to pay for drugs under clinical investigation and a final ruling on the matter is expected next month.

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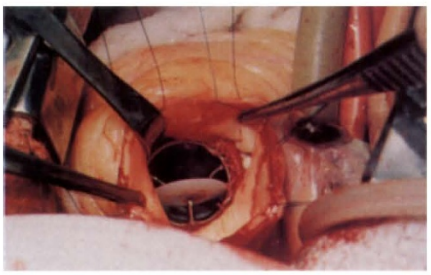
# Valve to save poor hearts

Using home-grown technology, medical researchers in India have developed a new mechanical heart valve that will be commercially available later this year for about one-third of the price of competing devices such as the Bjork–Shiley valve, which has been in use for more than 20 years. At that price, the valve is expected to have the greatest impact among some of the country's poorest communities. However, even if the performance of the new valve is demonstrated to be comparable to existing devices, its acceptance in wider medical circles could take some time.



**Surgery to insert new inexpensive mechanical heart valve from India.**

The new 'chitra' valve is expected to bring hope especially to an estimated 1.5 million children in the 6–18 age group who need replacement valves because their valves have been damaged by rheumatic heart disease — the single most common cause of valve replacement in India. A result of repeated (but untreated) throat infections, rheumatic heart disease is estimated to affect 5 out of every 1,000 children in India, and there are nearly 20,000 new patients needing heart-valve replacements each year. Most of them face premature death because they are too poor to afford the US$1,100 plus for the imported versions.

Weighing in at less than 5 grams, the chitra valve is said to be the lightest of the six or so commercially available mechanical heart valves. It has been tested in 298 patients who participated in a multi-centre clinical trial that began in India four years ago. The valve was initially tested in sheep.

The valve takes its name from the centre where it was developed, namely the Sri Chitra Tirunal Institute of Medical Science and Technology in Tiruvananthapu-