

Healthcare industry BW

Methadone for cancer treatment? Clinical trials are needed to prove the effectiveness of this opioid

Claudia Friesen, an oncologist at Ulm University Hospital, has achieved what many scientists dream of: she has made a discovery that has increased existing knowledge, and can be used to help people. People with cancers that are resistant to all conventional therapies who have been given methadone for pain relief in combination with conventional chemo- or radiation therapy, have reported that tumours have shrunk or disappeared completely. Clinical trials that provide evidence for this are not yet available. Professional associations warn of false expectations.

Editor's note:

According to a position statement published by the University of Ulm, Ulm University Hospital and the Comprehensive Cancer Center Ulm (CCCU) on 24th August 2016, which BIOPRO's editorial office has had in their possession since 5th December 2016, this article solely concerns basic research findings. Please refer to the comprehensive position statement (see *Downloads* section) of the Comprehensive Cancer Center Ulm (CCCU) for further details. Please also see *Downloads* section for a paper on a retrospective clinical trial on D,L methadone in glioma patients carried out in cooperation with the Charité in Berlin and published in early 2017.



Cancer researcher Dr. Claudia Friesen
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Through her contacts with cancer patients and doctors, Claudia Friesen is aware of about 750 cancer cases who have been treated with D,L-methadone, including 100 people who, if the medical textbooks were right, should already have died of the disease, but instead have greatly benefitted from the methadone treatment. The opiate has even been shown to be effective against glioblastoma, a highly malignant type of brain cancer. Many of these patients are delighted to talk about their experiences with methadone: tumours have shrunk and metastases disappeared. They have also reported a dramatic improvement in quality

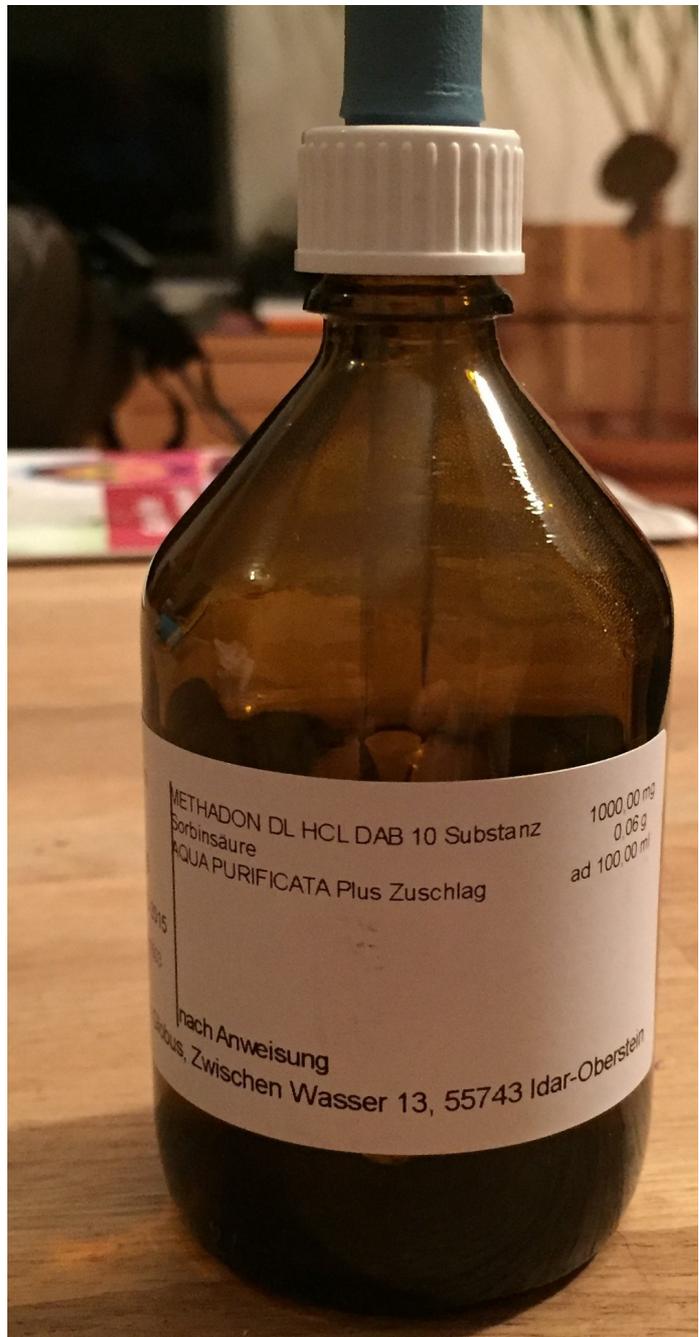
of life. In Germany, methadone can be prescribed by GPs or palliative physicians for the treatment of pain. Doctors prescribing methadone to treat cancer pain usually work closely with Friesen to discuss treatment options.

Methadone as a potential anti-cancer therapy

Friesen wants to bring “methadone into clinical practice to support and enhance conventional cancer treatments.” She has found that the synthetic opiate significantly improves treatment outcomes, overcomes resistance and does not attack healthy cells. Her findings could also be used to treat other cancers such as pancreatic cancer and certain forms of breast, ovarian and prostate cancer. In July 2015, Claudia Friesen heard of six glioblastoma patients whose tumour had completely regressed thanks to the painkiller methadone. Mainstream medicine does not believe that this is possible, but Friesen is convinced that this medical miracle is down to methadone.

Mamazone, a German breast-cancer patient self-help group with around 1,800 members, had the following comment to make when asked whether methadone should be considered an anti-cancer drug: “Why shouldn't D,L-methadone be used for treating metastases and solid tumours, rather than just for pain relief in advanced stages of cancer? Hope, be it false or legitimate, has no side effects; it is either fulfilled or it isn't.” Mamazome presented Friesen's work in the June issue of mamazome MAG magazine.

The oncologist has published and explained methadone's mechanism of action in scientific papers, and so far no one has questioned her findings. German Cancer Aid, which funded Friesen's research, also reported on Friesen's laboratory experiments with glioblastoma cells (“Methadon: Allroundtalent gegen Hirntumoren”, 30th September 2014).



Does methadone, which is commonly used as a pain relief in cancer patients, also cure cancers?
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There is no getting away from clinical studies

However, all this research is not grounds enough for methadone to be prescribed for cancer

treatment. Methadone is normally used to wean addicts off drugs such as heroin as it reduces the physical withdrawal symptoms that users experience when coming off hard drugs. Clinical trials involving human subjects are therefore needed to prove the efficacy and tolerability of methadone before regulatory approval for its use as an anti-cancer drug can be obtained. Friesen is well aware of these regulations and the requirement to carry out clinical trials. However, clinical trials are costly and take a long time, time which patients who have had all the possible kinds of conventional treatment do not have. Friesen explains that a phase II clinical trial costs between 1.2 to 1.5 million euros and takes between one and two years.

Ever since Friesen left the field of basic research and moved towards clinical application, she has faced major criticism, opposition and bad press from the ranks of large, established university medical centres. On 26th March 2015, the Neurooncology Working Group of German Cancer Aid (NOA) and the German Neurological Society (DGN) published a joint statement in which physicians warned: "To date, there is no evidence for the effectiveness of methadone in the treatment of gliomas. Apart from in clinical trials, the use of methadone is "not justified", and "has a plethora of unwanted adverse effects".

Medical associations: experimental data with no informative value

The joint statement referred to a "large number of inquiries related to the theme" on which "we are keeping an open mind" which, says Prof. Wolfgang Wick, explains why the statement was made public. Wick is the NOA spokesman and Medical Director of the Neurological Hospital and the National Centre of Tumour Diseases at Heidelberg University Hospital. He counters Friesen's criticism that no one contacted her prior to the press release on Ulm University Hospital's website by saying that "she was in fact contacted for the benefit of individual patients. We are also in contact with some of Dr. Friesen's oncology colleagues in Ulm to discuss further clinical developments." He also said that given the variety of therapeutic concepts available, NOA and DGN have no obligation to refute or substantiate Dr. Friesen's claim on the efficacy of methadone as an anti-cancer drug.

Hans-Jörg Hilscher, palliative doctor and GP from Iserlohn, finds the warnings about methadone utterly incomprehensible. He considers them lacking in substance, and refers to them, somewhat provocatively, as "eminence-based medicine". He knows more about methadone than anyone else. He has been using it since 1999 as pain relief for hospice patients who, as a consequence, lived longer than their prognoses led to believe and enjoyed a better quality of life than could be expected.

Methadone is battling a bad reputation

Hilscher used a combination of methadone and the cytostatic drug methotrexate, and found that cancer patients given such treatment did not develop fatal ascites and pleural effusions. In 2008, Friesen discovered by chance that methadone destroys cancer, and Hilscher, also convinced that methadone could be used for cancer treatment, has been working with her ever since. He believes that methadone is the opiate with the least adverse effects. Hilscher has spent many years developing a therapy concept using methadone. However, he knows of many colleagues who are afraid to prescribe it. Hilscher believes that a mixture of ignorance, bad publicity and economic interests has contributed to the drug's bad reputation.

Methadone is subject to the German Narcotics Act which requires doctors to fill in a special form when they prescribe methadone. Commercially available methadone tablets and solutions are only



Methadone is well suited for application in palliative care as it can be administered orally.

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licensed for opioid replacement therapy. "In order to produce D,L-methadone solutions and tablets, pharmacies have to use a recipe that makes selling methadone unprofitable. Pharmacies are forced to purchase large quantities of methadone to prepare the required solutions / tablets and are unable to sell the entire batch if methadone is not prescribed / bought regularly," says Hilscher. A 100 ml one-percent methadone solution, which is enough for six weeks' treatment, costs twelve euros. "No one is interested in publicising a drug that sells for so little," says Hilscher. Methadone is a fully synthetic opioid that is taken in relatively low doses: between 2 x 20 (i.e. 2 x 10 mg) and 2 x 35 drops for pain patients. Such a low dose

usually causes very few adverse effects, if any, only mild nausea and constipation. The doses of methadone taken as a heroin replacement are usually ten times higher.

Application for clinical trial

Meanwhile, researchers led by Prof. Thomas Seufferlein (medical director of the Department of Internal Medicine I at Ulm University Hospital) have started preparing an application for a clinical trial for colon cancer, the second most common type of cancer. This phase I/II study will study the effect of D,L-methadone on patients with histologically confirmed colorectal carcinomas. The main objective of the double blind randomised phase II trial is to monitor the progression-free survival of patients treated with D,L-methadone or placebos for 12 weeks.

A retrospective study assessing the effectiveness of D,L-methadone in glioma therapy produced no clear results. The study involving 20 patients was carried out in the Department of Neurosurgery at the Charité Hospital in Berlin. Dr. Marin Misch, a senior physician in the department, presented this non-interventional, patient-centred observational study at a meeting of the German Society of Neurosurgery in Freiburg in late October 2015. The study found that D,L-methadone could be combined with cancer therapies without any risk of elevated toxicity. In the early stages of D,L-methadone treatment, patients experienced moderate nausea, which disappeared within a month. However, data of scientific validity that prove the efficacy of D,L-methadone for treating gliomas can only be collected in a prospective, randomised trial.

Ethical dilemma for patients that do not respond to conventional therapies

The procedure required for obtaining approval for using methadone as an anti-cancer drug is not an alternative for cancer patients who have already been given all known effective treatments. Such trials compare a new anti-cancer drug with a placebo so that researchers can determine the positive and negative effects of the drug. Patients would therefore run the risk of being put into the control group and given the placebo instead of D,L-methadone, destroying their last fragile hope for improvement. This is an ethical dilemma for which there is currently no quick solution.

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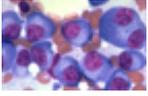
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- ▶ [Stellungnahme CCCU Methadon \(PDF ca. 23.43 KB\)](#)

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