# Drug designed to boost radiotherapy for hard-to-treat cancers taken safely by patients

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A new drug designed to make radiotherapy more effective in treating cancer has been given to patients while they are receiving radiation and shown to be safe, according to research presented today (Wednesday) at the 30th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Dublin, Ireland.

The drug, called 5-iodo-2-pyrimidinone-2'-deoxribose (IPdR), or ropidoxuridine, has the advantage that patients can take it in capsule form, as opposed to intravenously. When the drug enters the body, researchers believe it changes into an active form that can make cancer cells more susceptible to the effects of radiotherapy.

Results of US NCI trial #9882, presented by Dr. Timothy Kinsella from the Department of Radiation Oncology at the Warren Alpert Medical School of Brown University and Rhode Island Hospital in the USA, show that the drug has minimal side effects when given to patients with a variety of gastrointestinal cancers during the course of their radiotherapy.

Dr. Kinsella explained: "The aim of my research is to find better ways to treat patients with cancer, and specifically to develop ways to make radiation treatment safer and more effective.

"Previous research found a promising compound called iododeoxyuridine, or IUdR, that worked very well to improve the effectiveness of radiotherapy, but IUdR could only be given

intravenously and proved to have many side effects for patients.

"As a result, this new drug, IPdR, was developed. It's a prodrug that can be taken as a capsule and, once inside the body, it's converted into the active drug, IUdR.

"This trial is the first to test it out in patients while they are receiving radiation therapy, and the results suggest that it's safe with minimal side effects."

Dr. Kinsella and his colleagues tested the new drug in a group of 18 patients with advanced cancers including oesophageal, pancreatic, liver, bile duct, rectal and anal cancers. All had been referred for palliative radiotherapy.

Alongside their radiotherapy, patients were given a daily dose of the IPdR prodrug over 28 days. They were given blood tests to check on the levels of both the IPdR prodrug and the active IUdR drug at various points during their treatment. The dose of the prodrug was gradually increased, and patients were monitored for side effects.

Results of the trial suggest that IPdR can be safely given to patients up to a dose of 1200mg per day for 28 days without causing serious side effects. The results also suggest that this dose creates levels of the active IUdR drug in patients' blood that are high enough to have a radiosensitising effect.

Of the 18 patients on the trial, 14 could be assessed for any effect on their tumours with a CT or MRI scan 54 days after beginning the treatment. Among these patients, one had a complete response (disappearance of tumour), three showed a partial response (at least 30% reduction in the tumour targeted by radiotherapy), nine had stable diseases (no growth in the tumour) and one patient stopped treatment

because of an infection and had progressive disease (at least 20% growth in the tumour).

Dr. Kinsella added: "This clinical trial showed that when patients take IPdR at home before coming for radiation treatment, the level of IUdR in their bloodstream is high enough to make radiation more effective at killing cancer cells. It also showed that the dose of IPdR needed to achieve therapeutic levels of IUdR in the blood causes minimal side effects.

"However, this trial was with patients who had recurrent cancer and had already received a number of other cancer treatments. In newly diagnosed patients, it could be that we can safely use a higher dose and have a bigger effect on tumours."

Dr. Kinsella and his colleagues are already studying the effects of IPdR in patients receiving whole brain radiotherapy for cancer that has spread to the brain. Following this trial, plans are in progress to study the drug in patients who have been newly diagnosed with glioblastoma, an aggressive form of brain cancer.

Professor Eric Deutsch, professor of radiation oncology and head of the radiation oncology department and research unit at the Institut Gustave Roussy, Villejuif, France, is a member of the EORTC-NCI-AACR Symposium scientific committee and was not involved with the research. He said: "Radiotherapy is a vital element in treating many forms of cancer. This research is investigating whether the IPdR drug could make radiotherapy even more effective for more patients.

"In treating cancer patients, we must always consider the risks and benefits of any therapy. In this study, the risks of the IPdR drug were minimal, and the benefit was that it can be taken by patients at home. We don't have enough evidence yet on whether IPdR can improve

patient outcome, but we hope that this will become clearer as the research continues."

**More information:** Abstract no: 005, "Pharmacology of oral (PO) Ropidoxuridine in treating patients with advanced gastrointestinal cancer undergoing radiation therapy (RT) (NCT02381561)". Proffered papers, plenary session 2, Auditorium, 13:30 hrs, Wednesday 14 November 2018.

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