New cancer treatment slows progression of aggressive neuroendocrine tumors, study finds

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Simron Singh, a medical oncologist at Sunnybrook Health Sciences Centre and associate professor in the Temerty Faculty of Medicine, is principal investigator of a study that found that radioligand therapy significantly reduces the risk of advanced neuroendocrine tumor progression and death. Credit: Kevin Van Paassen, Sunnybrook Health Sciences Centre

A novel approach for early cancer treatment known as radioligand therapy (RLT) has been shown to significantly reduce the risk of advanced neuroendocrine tumor progression and death, according to research led by scientists at Sunnybrook Health Sciences Centre and the University of Toronto.

Results of the multi-center clinical trial, which were published in *The Lancet*, provided evidence for the first time that RLT—when applied in the early stages after a patient's diagnosis—slowed down the progression of aggressive grade 2 and 3 neuroendocrine tumors of the gastrointestinal tract.

The treatment was shown to extend the average time of "progression-free survival" from approximately 8.5 months to 22.8 months.

"This is the first study to show the effectiveness of RLT as the 'first-line' treatment with advanced uncurable cancer, or any cancer," said the study's global principal investigator Simron Singh, a medical oncologist at Sunnybrook and associate professor in the department of medicine at U of T's Temerty Faculty of Medicine. "This trial is groundbreaking not only for patients with neuroendocrine cancers, but for all cancer patients as it has implications for the practice of cancer treatment broadly."

Singh described RLT as a "game changer" in the treatment of cancer, which has traditionally been carried out by surgery, drugs or radiation.

"While it's technically radiation, it is given via a chemotherapy route through the blood until it reaches the precise location of the tumor," said Singh, who is also an affiliate scientist at Sunnybrook Research Institute and co-founder of the Susan Leslie Clinic for Neuroendocrine Tumors at Sunnybrook's Odette Cancer Centre.

RLT involves injecting radioactive isotopes—in this case, the drug

lutathera—through an IV. This method targets specific cancer cell receptors, delivering precise radiation to kill cancer cells while preserving healthy tissue.

The study evaluated the use of RLT earlier as a first-line (or "up front") treatment for patients newly diagnosed with grade 2 or 3 advanced gastrointestinal neuroendocrine tumors. Although neuroendocrine cancer is uncommon, incidence is rising rapidly, and few treatments exist for patients. This cancer is resistant to most therapies, making it challenging to treat.

The results confirm the clinical benefit of earlier use of RLT for patients diagnosed with aggressive and life-threatening tumors, said Singh. "This is the next step in personalized targeted cancer therapy for patients, focused on more effectively killing cancer cells, while limiting the damage to surrounding healthy tissues."

Further investigations of RLT as a therapeutic option are ongoing to evaluate overall survival and long-term safety, which will better define next steps for how this therapy will change cancer treatment world-wide.

The multi-site trial included investigators and participants from Canada, the United States, France, Germany, Italy, Netherlands, South Korea, Spain and the UK. An overview of the results was presented at the 2024 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Cancers Symposium in January 2024.

More information: Simron Singh et al, [177Lu]Lu-DOTA-TATE plus long-acting octreotide versus high-dose long-acting octreotide for the treatment of newly diagnosed, advanced grade 2–3, well-differentiated, gastroenteropancreatic neuroendocrine tumours (NETTER-2): an open-label, randomised, phase 3 study, *The Lancet* (2024). DOI: 10.1016/S0140-6736(24)00701-3

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