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Cancer patients treated in world-first clinical trial of Canadian viral therapy

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Canadian researchers have launched the world's first clinical trial of a novel investigational therapy that uses a combination of two viruses to attack and kill cancer cells, and stimulate an anti-cancer immune response. Previous research by this team and others worldwide suggests that this approach could be very powerful, and could have fewer side effects than conventional chemotherapy and radiation, although it will take years to rigorously test through this trial and others.

The therapy was jointly discovered and is being developed by Dr. David Stojdl (Children's Hospital of Eastern Ontario, University of Ottawa), Dr. Brian Lichty (McMaster University) and Dr. John Bell (The Ottawa Hospital, University of Ottawa), and their respective research teams and colleagues. The clinical trial, which is funded by the Ontario Institute for Cancer Research and coordinated by the NCIC Clinical Trials Group, is expected to enroll up to 79 patients at four hospitals across Canada. Up to 24 patients will receive one of the viruses and the rest will receive both, two weeks apart.

Christina Monker, 75, a former nurse from Rockland, Ontario, is one of the first patients treated in the trial. She was diagnosed with cancer in 2012 and, despite six weeks of radiation therapy and two rounds of chemotherapy, the cancer spread to both her lungs. After completing another 30 rounds of chemotherapy, she enrolled in the trial at The Ottawa Hospital and was treated on June 2, 2015.

"The nausea of chemotherapy was worse than I ever could have

imagined, but with the viral therapy I just felt like I had the flu for a couple of days, and the symptoms were easily managed," said Ms. Monker. "It is too soon to know if I may have benefited from this therapy, but I'm very glad to contribute to this important research that could improve care for others."

The idea of using viruses to treat cancer has been around for more than a century, with sporadic reports of cancer patients experiencing remarkable recoveries after viral infections. However, it is only in recent years that viral therapy has begun to be developed and tested in a rigorous way. Drs. Bell, Lichty and Stojdl began investigating viral therapies for cancer nearly 15 years ago when they worked together at The Ottawa Hospital.

"We found that when normal cells become cancerous, it's like they are making a deal with the devil," explained Dr. Bell, a senior scientist at The Ottawa Hospital and professor at the University of Ottawa. "They acquire genetic mutations that allow them to grow very quickly, but these same mutations also make them more susceptible to viruses."

The two viruses being tested in this clinical trial are called MG1MA3 and AdMA3. MG1MA3 is derived from a virus called Maraba, which was first isolated from Brazilian sandflies, while AdMA3 is derived from a common cold virus called Adenovirus. Both of these viruses have been engineered to stimulate an immune response against cancer cells that express a protein called MAGE-A3, but the Maraba virus also achieves an extra layer of anti-cancer activity by replicating inside many kinds of cancer cells and killing them directly. These viruses are manufactured in specialized facilities at The Ottawa Hospital and McMaster University.

"The idea behind this trial is to use the Adenovirus to prime the patient's immune system to recognize their cancer, and then use the Maraba virus

to directly kill their cancer and further stimulate their immune system to prevent the cancer coming back," said Dr. Brian Lichty, associate professor at McMaster University. "We're enthusiastic about the potential of this unique therapy."

"We're very excited about this first clinical trial," said Dr. Stojdl, senior scientist at the Children's Hospital of Eastern Ontario and associate professor at the University of Ottawa. "We're continuing to push very hard to develop a suite of biological therapies with the goal of launching similar trials tailored to other types of tumours, including brain cancer and several devastating childhood cancers."

Viral therapies are one component of a growing field of cancer research that seeks to use biological materials (including cells, genes, antibodies and viruses) to attack cancer cells and stimulate an anti-cancer immune response. This field of research has been called biotherapy or immunotherapy. Dr. Bell and his colleagues recently launched the $60M BioCanRx network to advance this area of research.

The Maraba virus is an important part of a broad biotherapeutics clinical trial development program in Canada that is combining viruses and vaccines with standard and emerging therapies to treat different types of tumours. Drs. Lichty, Bell and Stojdl and their institutions, in cooperation with the Fight Against Cancer Innovation Trust, have formed Turnstone Biologics in order to engage the private sector and to help fund further clinical trials.

"Immunotherapy is a very exciting field of cancer research, with antibody-based therapies showing the most promise in clinical trials so far," said Dr. Derek Jonker, the overall lead for the clinical trial, a medical oncologist at The Ottawa Hospital and a professor at the University of Ottawa. "Viral therapies have also shown promise in laboratory studies, but it is too soon to know what impact they may have

on patients. This clinical trial will help us find out and we're very grateful to the patients who have participated."

"Ontario is pleased to support innovative research through the Ontario Institute for Cancer Research," said Reza Moridi, Ontario Minister of Research and Innovation. "Our investments have enabled our researchers to be at the forefront of this new therapy.

Immunotherapy has the potential to vastly improve the way cancer is treated, and is another example of how research investment brings tangible benefits to Ontarians and people around the world."

"The NCIC Clinical Trials Group is very pleased to conduct this trial, which offers a potential new therapeutic approach for cancer patients that has been developed by Canadian researchers," said Dr. Janet Dancey, director, NCIC Clinical Trials Group and professor at Queen's University in Kingston.

"Our Government is committed to investing in research that will accelerate efforts to find a cure for cancer, a disease that kills thousands of Canadians each year. The clinical trial announced today represents an innovative approach to treating cancer. We are proud to have contributed to the development of this therapy and wish the researchers and clinicians every success as they carry out this important study," said the Honourable Rona Ambrose, Canada's Minister of Health.

In addition to The Ottawa Hospital, the clinical trial is also taking place at the Juravinski Cancer Centre of Hamilton Health Sciences (under the leadership of Dr. Sebastien Hotte), Princess Margaret Cancer Centre of the University Health Network in Toronto (under the leadership of Dr. Albiruni R A Razak) and the Vancouver Centre of the BC Cancer Agency (under the leadership of Dr. Daniel Renouf).

The trial was approved by Health Canada, the Ontario Cancer Research Ethics Board and the BC Cancer Agency Research Ethics Board. Further details about the trial are available at clinicaltrials.gov. Patients wishing to participate in the trial should speak with their own oncologist and ask for a referral to one of the participating hospitals. Further details for patients at The Ottawa Hospital are available online.

While this trial is primarily funded by the Government of Ontario through the Ontario Institute for Cancer Research, many other funding organizations have also supported the research of Drs. Bell, Lichty and Stojdl, including The Ottawa Hospital Foundation, CHEO Foundation, Canadian Cancer Society, Terry Fox Research Institute, Canadian Institutes of Health Research, Ontario Ministry of Research and Innovation, Canada Foundation for Innovation, Ottawa Regional Cancer Foundation, Hair Donation Ottawa, Angels of Hope, BioCanRx, Pancreatic Cancer Canada, NAV Canada and several philanthropic donors.

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