

New pretargeted radioimmunotherapy for colorectal cancer

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Investigators at SNM's 58th Annual Meeting are presenting results from a phase 1 clinical trial for a cancer therapy that has the potential to kill colorectal tumors with less destruction of healthy tissue. Further research could lead to the use of this radioimmunotherapy to eliminate residual cancer after surgery or as a standard treatment to keep tumors from returning or spreading to other organs.

"Compared to the conventional way of guiding radiation to tumors with radiolabeled antibody, pretargeted radioimmunotherapy offers an attractive potential alternative because the delivery of therapeutic isotope is rapid and is separated from the long antibody delivery process, thereby reducing the harmful effects of radiation to the body, especially the bone marrow," says Rafke Schoffelen, MD, scientist of the study at Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. "This results in an optimal scheme with maximum therapeutic effect and minimal side effects."

According to the American [Cancer](#) Society it is estimated that more than 141,200 Americans in 2011 will be diagnosed with colorectal cancer, and 48,000 will die of the disease. Colorectal cancer is currently the third most commonly diagnosed cancer and the third leading cause of [cancer death](#) for both men and women across the country. This form of cancer develops in the colon and rectum, usually as a result of [polyps](#), or abnormal growths, that extend from mucous membranes in the lower gastrointestinal tract. Once cancer is detected, the most common treatments are surgery and chemotherapy, but chemotherapy is

associated with many side effects, some of them serious and lifelong. This pretargeted radioimmunotherapy is engineered to be an effective alternative with far fewer adverse effects.

In recent years the development of radioimmunotherapy has led to increasingly targeted cancer therapies that combine antibodies pinpointing specific physiological processes of the cancer and [medical isotopes](#) that deliver a dose of radiation to the cancer tissue. Pretargeted radioimmunotherapy takes this a step further by breaking the therapy into two phases. In the first phase, an antibody is infused that recognizes both an antigen from the tumor and the building blocks of proteins that serve as a vehicle for the radioisotope. When the antibody has cleared the rest of the patient's system, leaving only the tumor-bound antibody, a second phase is administered in the form of an injected small protein labeled with the medical isotope. The drug binds with the already tumor-bound antibody and delivers the radiation dose. The fraction of the drug that is not bound is quickly cleared from the rest of the body by the kidneys and out through the urine.

The objective of this study—the first of its kind to treat patients with metastatic, or spreading, colorectal cancer with pretargeted radioimmunotherapy—was to improve patients' prognosis without compromising their quality of life. It is conducted in collaboration with Garden State Cancer Center, Belleville, Immunomedics Inc. (NASDAQ: IMMU) and IBC Pharmaceuticals Inc. of Morris Plains, N.J., developers of the pretargeting mechanism and reagents.

First, patients were administered a test-cycle to map the path and predict the radiation dose of the subsequent therapy injection. The antibody, TF2, was infused followed by the small protein, IMP288, carrying a non-therapeutic isotope, ^{111}In , which was measured by whole-body planar and single photon emission computed tomography imaging. Patients were then administered TF2 again, and the therapeutic isotope and agent

¹⁷⁷Lu-IMP288. Research showed effective targeting of tumors and minimal healthy tissue damage, which could lead the way for further studies with higher or multiple dosing strategies and greater targeting of cancer tissue.

More information: Scientific Paper 358: R. Schoffelen, O. Boerman, W. van der Graaf, C. van Herpen, R. Sharkey, W. McBride, C. Chang, E. Rossi, D. Goldenberg, W. Oyen, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; Garden State Cancer Center, Belleville, NJ; Immunomedics, Inc., Morris Plains, NJ; IBC Pharmaceuticals, Morris Plains, NJ; "Phase I clinical study of the feasibility of pretargeted radioimmunotherapy (PT-RAIT) in patients with colorectal cancer (CRC): First results," SNM's 58th Annual Meeting, June 4-8, 2011, San Antonio, TX.

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