

For Colorectal Cancer Awareness Month, Take a Look at Novel Treatment Studies

Dana-Farber researchers explore CAR-T therapy and next generation immunotherapy to target colorectal cancer.

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Colorectal cancer is the 3rd most common cancer among men and women of all ages in the United States and is on track to be the leading cause of cancer death in adults under 50 by 2030. The alarming rise of colorectal cancer in people younger than 50 prompted the U.S. Preventive Services Task Force to lower the colorectal cancer screening age from 50 to 45 in 2021. [Dana-Farber Cancer Institute](#) recognizes the need for new therapies and is committed to finding more effective ways to treat colorectal cancer.

[Benjamin Schlechter, MD](#), a senior physician in the [Gastrointestinal Cancer Treatment Center at Dana-Farber](#), is leading two studies to investigate novel treatment options for colorectal cancer patients. “Translation of ideas from the laboratory to clinical medicine remains one of the huge hurdles. It’s fantastic to have multiple promising trials underway for patients with colorectal cancer,” said Schlechter.

Next-Generation Immunotherapy Shows Activity in Common Type of Colorectal Cancer

One avenue of clinical research at Dana-Farber includes [a study testing a combination of two next-generation immunotherapy drugs](#). The phase 1 trial included patients with metastatic colorectal cancer who had already been treated with several lines of drugs, including prior immunotherapies. These patients all had tumors classified as microsatellite stable (MSS), which account for most colorectal cancers. In previous studies, first generation immunotherapies have had little effect on this type of tumor.

The two next-generation immunotherapy drugs in the trial are designed to release the brakes on the immune system in two different ways. One drug, botensilimab, aims to unleash T-cells against the cancer by targeting one such brake, an immune checkpoint protein called CTLA-4. CTLA-4 is a

receptor found on T-cells and regulates T-cell activation. The other drug, balstilimab, frees the immune system to attack the cancer by blocking PD-1, another immune checkpoint protein. The drug combination showed promising clinical activity in these patients who otherwise had few treatment options. The main population of patients who benefited from the combination were those who did not have active metastatic cancer in their liver.

Two randomized phase 2 trials in patients with MSS colorectal cancer are opening in the coming weeks.

“This is the first ever immune therapy in MSS metastatic colorectal cancer to show any responses let alone durable and profound responses,” said Schlechter.

Novel CAR-T Therapy Specifically Targets Colorectal Cancer

Another research avenue at Dana-Farber involves a phase 1 trial of a cell therapy called GCC19CAR-T. CAR-T therapy involves removing a patient’s own immune cells, called T-cells, genetically enhancing them to recognize and target the specific form of cancer, and then reinfusing the cells. While effective at treating certain blood cancers, so far, CAR-T therapies have not worked for solid tumors, such as colorectal cancer, in part because it has been extremely difficult to uniquely target tumor cells.

GCC19CAR-T specifically targets colon cancer by binding to a protein called GCC (guanyl cyclase C) that is thought to be present in 70-80% of colon cancers. In addition, the GCC specific CAR-T-cells are combined with CD19 CAR-T-cells to create a sling-shot effect that causes the GCC T-cells to activate and proliferate in the bloodstream. They then flow into the tumor where they bind to and kill the cancer cells. The trial is enrolling patients now.

“This therapy has the potential to introduce CAR-T to a significant number of patients with refractory colorectal cancer,” said Schlechter. “Because of its specificity to the cancer, it could enable a potent immune response without causing injury to healthy tissue.”

In an upcoming event hosted by Dana-Farber, immunotherapy, and its potential in treating colorectal cancers, will be featured in a keynote address by Myriam Chalabi, MD, PhD. Chalabi practices medical oncology in Amsterdam, Netherlands and is lead investigator of several immunotherapy trials in gastrointestinal cancers. She was a featured speaker at the [Young-Onset Colorectal Cancer Center](#) Patient and Family Forum in Boston on March 4, 2023.

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