Expanding immunotherapy options for patients with advanced breast and colorectal cancer

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Dr. Sarbajit Mukherjee. Credit: Roswell Park Cancer Institute

Two Roswell Park Comprehensive Cancer Center oncologists will discuss promising strategies for making breakthrough immunotherapies

work for more patients at the annual meeting of the American Association for Cancer Research (AACR) in New Orleans, Louisiana, on Monday, April 11. Both presentations were accepted as late-breaking abstracts and report findings from clinical trials that advance a novel immunotherapy platform in development at Roswell Park under the leadership of Pawel Kalinski, MD, Ph.D., involving modulation of key proteins known as chemokines.

Chemokine-modulating infusion increases local infiltration of immune cells into colorectal tumors

On April 11, from 9 a.m. to 12:30 p.m. CT, Sarbajit Mukherjee, MD, MS, Assistant Professor of Oncology in the Department of Medicine and member of the Tumor Immunology and Immunotherapy Program at Roswell Park, will present initial results of a phase 2 study evaluating a chemokine-modulatory regimen in patients with colorectal cancer metastatic to the liver.

"Somewhere between 20% and 50% of patients with metastatic colorectal cancer will develop liver metastases, which are typically resistant to immune checkpoint inhibitors and carry a poor prognosis," says Dr. Mukherjee. "We developed a systemic chemokine modulatory regimen that was effective in turning nonresponsive 'cold' tumors into inflamed 'hot' tumors more likely to respond to immunotherapy."

In this phase 2 study, Dr. Mukherjee, together with several other Roswell Park colleagues, treated 19 patients with recurrent or advanced colorectal cancer that had spread to the liver using a combination of two chemokine-activating drugs, rintatolimod (brand name Ampligen) and interferon alfa-2b (brand name Intron A), in addition to an anti-inflammatory drug, celecoxib. Treatment was well tolerated, the team reports, with the most common side effect being fatigue.

After treatment, the researchers found, patients' tumors evidenced a significant increase in cancer-fighting cells called cytotoxic T lymphocytes, suggesting that this chemokine-modulatory regimen could be used to improve immunotherapy outcomes for patients with colorectal cancer.

Same chemokine-modulating infusion assessed in patients with triple-negative breast cancer

On April 11, from 1:30 to 5 p.m. CT, Shipra Gandhi, MD, Assistant Professor of Oncology specializing in breast cancer in the Department of Medicine, will share results of a study that evaluated the feasibility of the same chemokine-modulation regimen for the treatment of patients with advanced triple-negative breast cancer, followed by optional pembrolizumab immunotherapy as a follow-up treatment.

"Current immunotherapies show limited effectiveness in metastatic triple-negative breast cancer, and are approved only in combination with chemotherapy at this time—and only for the small subset of patients whose tumors express high levels of PDL1, an immune marker that predicts response to immunotherapy," says Dr. Gandhi. "In this study, our systemic chemokine-modulatory regimen induced selective local infiltration of desirable immune cells, including CD8+ T cells known to be associated with improved breast cancer outcomes, into the tumors of patients with metastatic triple-negative breast cancer, without inducing suppressive Treg cells."

In this early phase 1 trial, Dr. Gandhi and colleagues investigated the effectiveness of this chemokine-modulation strategy in eight patients with metastatic triple-negative breast cancer. Treatment was generally well tolerated, the team reports, and an increase in the number of cancer-fighting immune cells was observed, suggesting that chemokine therapy

can help patients with metastatic breast cancer become more responsive to immunotherapy.

Strategy in development for more than a decade

Traditional immunotherapy often does not work in patients with advanced colorectal or breast cancer, as these tumors are usually cold, or noninflamed. Chemokines are proteins with the ability to recruit helpful immune cells to fight cancers to cancer tissues, which can turn these cold tumors hot, rendering them more receptive to immunotherapy and other forms of cancer treatment.

Dr. Kalinski, Chair of the Department of Immunology and Chief of Translational Immuno-Oncology at Roswell Park, developed this innovative approach over the last 15 years.

Roswell Park's platform for chemokine modulation is specific to tumors, meaning that the treatments can generate immune responses only in cancer tissues and not in normal, healthy tissue. Rintatolimod and interferon alfa-2b selectively activate chemokines in the tumor microenvironment, which in turn attracts desirable cancer-fighting immune cells to the tumor and improves responses to immunotherapy.

This unique chemokine-activating regimen, the authors note, can be used as a systemic intravenous infusion in patients with multiple tumor lesions or tumors that aren't accessible to direct injections. In these phase 1 and 2 clinical trials, the combination showed low toxicity and few side effects. Future Roswell Park studies will build upon these efforts to make tumors that are typically treatment-resistant more sensitive to immunotherapy.

Provided by Roswell Park Cancer Institute