

New Research in the Fight Against Ovarian Cancer

University of Colorado scientist Benjamin Bitler leads a team looking at overcoming resistance to standard ovarian cancer treatments.

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[Ovarian cancer](#) is one of the leading causes of cancer death among women, with nearly 20,000 new diagnoses each year and around 12,740 deaths from the disease estimated in 2024, according to the [American Cancer Society](#).

Researchers at the [University of Colorado Cancer Center](#) have recently published two research papers on novel therapeutic approaches for ovarian cancer, looking for new treatments to approach disease that doesn't respond well to chemotherapy or targeted therapy.

"We're working to develop novel therapeutics to address critical needs in ovarian cancer care," says researcher and CU Cancer Center member [Benjamin Bitler](#), PhD. "In breast cancer and many other cancers, we have multiple therapies in our toolbox to use against them. In ovarian cancer, it's much more limited."

Targeting tryptophan catabolism

Published in March in the journal [Cancer Research Communications](#), one of the new CU Cancer Center-led studies looks at the role of the amino acid tryptophan in how a patient's disease will respond to chemotherapy.

"Ovarian cancer is a disease of recurrence — almost 80% of all patients will recur at some point," Bitler says. "Our thought is that instead of curing cancer, which is a very high bar to cross, could we extend disease-free intervals to make the time between primary chemotherapy and recurrence longer? That's the bar we're shooting for."

The research looks specifically at a process known as tryptophan catabolism, in which tryptophan is broken down into smaller molecules as part of the metabolic process. Since an abundance of tryptophan can be used by cancer cells to grow and spread, inhibiting the catabolic process can help in preventing cancer from returning after chemotherapy.

“Previous research has shown not only that tryptophan catabolism is involved in promoting tumor progression, but also that immune cells in the tumor microenvironment undergo tryptophan catabolism to deplete tryptophan,” Bitler says. “T cells are then able to expand and react to the tumor in a way that causes an anti-tumor response. We wanted to find out if we could get some help from the host immune system to extend disease-free intervals by targeting tryptophan catabolism and promoting an immune response.”

Moving toward a clinical trial

With promising results from their laboratory models and ovarian cancer cell lines, Bitler and his fellow researchers — including CU Cancer Center member [Jennifer Richer](#), PhD — are looking toward launching a clinical trial of the tryptophan catabolism inhibitor, an oral medication. It’s an especially promising treatment for patients with ovarian cancer that does not have BRCA mutations, as those cancers already respond well to targeted cancer drugs called PARP inhibitors.

“Patients who aren’t BRCA-mutated aren’t eligible for PARP inhibitors, but our vision is that maybe they would be eligible for this tryptophan catabolism inhibitor,” Bitler says. “A person would undergo chemotherapy and then be given this as a maintenance dose. Everyone would still get the same six cycles of chemotherapy, but if you’re not BRCA-mutated, we don’t currently have any options for a maintenance treatment.”

When PARP inhibitors stop working

Patients with BRCA-mutated ovarian cancer that does respond to PARP inhibitors face another problem: Most eventually develop a resistance to the targeted treatment. CU Cancer Center researchers contributed to research published in May in the journal [Molecular Cancer Therapeutics](#) that showed that inhibiting groups of proteins known as EHMT1 and EHMT2 can stop that resistance from happening, allowing patients to continue to receive therapeutic benefit from PARP inhibitors.

“We found that by targeting the epigenetic environment of these PARP inhibitor-resistant cells, we can cause tumor regression,” Bitler says. “They regress in a way that would indicate an immune activation of the cells, or that the tumor cells are becoming more susceptible to immune surveillance.”

Bitler worked with CU Cancer Center member Edward Chuong, PhD, an expert on the human genome, and MD/PhD student Lily Nguyen, PhD, on the study, which found that a part of the genome becomes reactivated when treated with the EHMT2 inhibitor, promoting an inflammatory, anti-tumor response in the cancer cells.

“Our expectation would be that, at least initially, when a patient develops PARP inhibitor resistance, they would go on this EHMT2 inhibitor,” Bitler says. “We are also looking at what

happens when we combine this drug with PARP inhibitors in the early stages — can we prevent that resistance from ever even occurring? If we can answer that question, we may be able to shift the inhibitor even further forward, into a front-line or a second-line therapy.”

New treatment paths

Bitler sees his team’s research and similar studies as building on the successes of the past while looking ahead to new treatment options for ovarian cancer. He points out that the inhibitors discussed in these studies have been tested in laboratory models of ovarian cancer and still need to be tested in clinical trials. They are not yet available to treat patients.

“We’ve come a long way,” he says. “PARP inhibitors were approved in 2014, and it was one of the first new, approved targeted therapy in ovarian cancer. PARP inhibitors represented the idea of precision medicine: ‘We understand what your genetics are, so we’re going to prescribe this drug to you because we know it will work well with your genetics.’

“But unfortunately, we have not been able to add much to our repertoire beyond PARP inhibitors,” Bitler continues. “Any new therapies, especially ones that are moving into or currently are in clinical trials, offer an incredible opportunity to expand the repertoire of therapies we can use to target this devastating disease.”

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