

Ludwig Cancer Research and CRI initiate clinical trial of immunotherapy for ovarian cancer

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Ludwig Cancer Research and the Cancer Research Institute (CRI) have launched a Phase 1/2 clinical trial of combination immunotherapy for advanced ovarian cancer. The international, multicenter trial is led by George Coukos, director of the Ludwig Institute for Cancer Research, Lausanne and Brad Monk, director of Gynecologic Oncology at St. Joseph's Hospital and Medical Center. The study is being conducted through the CVC Trials Network, which is jointly managed by Ludwig and CRI, in collaboration with MedImmune, the global biologics research and development arm of AstraZeneca, and the biopharmaceutical company VentiRx Pharmaceuticals Inc.

"Ludwig has long supported the design and evaluation of new therapeutic strategies to improve the treatment options available to [cancer patients](#)," said Jonathan Skipper, Ludwig's executive vice president of Technology Development. "Employing immunotherapies in combination holds great promise in that endeavor. We are proud to be a part of this effort to bring investigational drugs being developed by different commercial partners to a single clinical trial and improve the standard of care for recurrent [ovarian cancer](#), a disease for which patients today have few treatment options."

The open-label trial is evaluating the combination of MedImmune's investigational antibody [cancer](#) drug durvalumab, a PD-L1 inhibitor, and VentiRx's investigational TLR8 agonist motolimod added to

chemotherapy in locally advanced or recurrent ovarian cancers that have become resistant to platinum chemotherapy. Both of the investigational drugs have been found in other studies to have acceptable safety profiles when used alone.

The researchers expect that motolimod's activation of TLR8 will create conditions within tumors that are optimal to enhancing the effects of durvalumab. Further, when given with chemotherapy, motolimod could boost immune responses against cancer cells that are not engaged by durvalumab by helping the [immune system](#) "see" cancer antigens. Since the two immunotherapies work in distinct ways, they could have additive effects, inducing more potent and durable anti-tumor immune responses.

"This study is a good example of what's possible when researchers have access to new therapies and are permitted to test hypotheses supported by the most recent science," said Ludwig Lausanne director George Coukos. "We are hopeful that the combined therapies we are testing in this trial will be of great benefit to ovarian cancer and other cancer patients."

Patients enrolled in the trial will be treated with the chemotherapeutic drug pegylated liposomal doxorubicin (PLD), which is the current standard of care for ovarian cancer after the failure of platinum therapy. They will also receive durvalumab and motolimod, with the Phase 1 and 2 portions of the trial running successively. The primary objective of the Phase 1 cohort of the study is to evaluate the safety and optimal dosage of the combination. The Phase 2 cohort of the trial will measure the efficacy of the treatment by evaluating the number of patients whose tumors have not progressed at six months.

Durvalumab is an investigational human monoclonal antibody directed against programmed death ligand-1 (PD-L1). PD-L1 expression enables tumours to evade detection from the immune system through binding to

PD-1 on cytotoxic T lymphocytes. Durvalumab blocks PD-L1 interaction with both PD-1 and CD80 on T cells, countering the tumour's immune-evading tactics. Durvalumab is being developed, alongside other immunotherapies, to empower the patient's immune system and attack the cancer. Durvalumab is being investigated in an extensive clinical trial program, as monotherapy or in combination with tremelimumab, in NSCLC, bladder, head and neck, gastric, pancreatic, HCC and blood cancers.

Motolimod binds and activates Toll-like receptor 8 (TLR8), which is found in a variety of immune cells and serves as a key initiator of the [innate immune response](#). Notably, it is expressed by myeloid dendritic cells, which help direct and boost T cell responses against infectious agents and cancers. Motolimod has been shown to be safe when combined with PLD in a previous study on ovarian cancer, with evidence of clinical benefit. The motolimod-PLD combination is currently under evaluation in a large, randomized, placebo-controlled phase 2 clinical study in patients with ovarian cancer.

"This clinical trial is part of a larger clinical research program supported by Ludwig and CRI to speed the evaluation of novel cancer immunotherapies, alone or in combination with other cancer drugs," said Adam Kolom, managing director of CRI's Clinical Accelerator, which funds the trials. "All of the studies have, as additional objectives, the collection of genetic and immunologic data derived from clinical samples that are obtained from patients. Such information will provide clues to the impact of the evaluated therapies and suggest refined or new strategies for treating cancer."

Provided by Ludwig Institute for Cancer Research

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