First Patients Dosed in Phase 2 Platform Clinical Trial Testing Novel Immunotherapy Combinations in Highly Malignant Ovarian Cancer

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The following is a press release from Ovarian Cancer Research Alliance and Cancer Research Institute:

- *Patients with ovarian cancer of the high-grade serous carcinoma subtype and that no longer respond to treatment with platinum-based therapy will receive a PD-L1-blocking antibody along with one of two antibody-drug conjugates targeting overexpressed receptor tyrosine kinases in the first two cohorts of this study*
- *Multiple sites across Canada and the U.S. open in 2022*
- *Combination immunotherapy may offer hope to the 80 percent of patients with this type of ovarian cancer who relapse and eventually succumb to the disease*
- *Cohorts A and B of this platform study are enrolling patients*

NEW YORK, May 11, 2022 — The Cancer Research Institute (CRI) and Ovarian Cancer Research Alliance (OCRA) announced today that the first patients have been dosed in their new multi-center platform clinical trial testing novel cancer immunotherapy combinations in patients with a common and highly aggressive form of ovarian cancer that has become resistant to treatment with platinum-based chemotherapy.

Currently, the majority of ovarian cancers – upwards of 75 percent – are of the subtype “high-grade serous carcinoma,” which is the type being treated in this phase 2 study. While most patients with this malignant ovarian cancer subtype initially respond to standard cytotoxic therapies, more than 80 percent will relapse and succumb to the disease within five years. New treatments are urgently needed for this deadliest of gynecological cancers, which is diagnosed in more than a quarter-million women worldwide each year according to World Health Organization estimates.

This phase 2 trial titled, “Immunotherapy Platform Study in Platinum Resistant High Grade Serous Ovarian Cancer (IPROC)” (NCT04918186), is co-funded by CRI and OCRA and is sponsored by CRI clinical partner the Canadian Cancer Trials Group (CCTG), and is open and actively recruiting patients to sites in Canada and, in the second half of 2022, will open sites in the United States. Overall, up to 60 patients are planned to be enrolled in this platform study with up to 40 patients in these two initial cohorts.

This clinical trial is using an adaptive platform study design that utilizes a single master protocol that allows for multiple treatments to be evaluated in different groups of patients, or cohorts, from the same patient population. Such a study design offers flexibility in that different treatments can be evaluated in different cohorts, treatment regimens can be modified between cohorts, and treatment selection criteria can be customized for a specific cohort.

Immunotherapy as monotherapy in treating patients with this aggressive type of ovarian cancer has not resulted in improvement in patient outcomes. In contrast, a recent randomized Phase 2 trial led by Dmitriy Zamarin, M.D., Ph.D., a member of the Cancer Research Institute Drug Selection Committee and study chair on the IPROC platform trial, demonstrated a three-fold improvement in overall response rates among ovarian cancer patients treated with a combination of immunotherapies compared to patients treated with a single immunotherapy.

“The IPROC trial builds upon the results seen in positive immunotherapy combination studies in ovarian cancer, and was designed in collaboration with our partners to explore each patient’s immunological response to determine which combinations result in the greatest patient benefit and why they are more effective than other combinations,” said Jay Campbell, managing director of the Anna-Maria Kellen Clinical Accelerator and Venture Fund at the Cancer Research Institute.

Patients with high grade serous ovarian cancer that is refractory or resistant to platinum-based cytotoxic therapy will be assigned to one of two cohorts testing novel immunotherapy combinations with drugs supplied by AstraZeneca and BioAtla, Inc.: Cohort A will receive AstraZeneca’s PD-L1-blocking antibody durvalumab (IMFINZI®) in combination with BioAtla’s BA3011 (mecbotamab vedotin), a conditionally active antibody-drug conjugate targeting AXL, a receptor tyrosine kinase that is overexpressed across many solid tumor types, while Cohort B will receive durvalumab in combination with BioAtla’s BA3021 (ozuriftamab vedotin), a conditionally active antibody-drug conjugate targeting ROR2, another receptor tyrosine kinase that is overexpressed in solid tumors. As part of the eligibility evaluation process, patients will be screened for expression levels of AXL or ROR2 and eligible patients will be assigned to the appropriate cohort accordingly.

“Ovarian cancer patients are in dire need of additional treatment options, and partnering with the Cancer Research Institute on this innovative platform trial is a crucial step in our efforts to hasten drug development,” said Audra Moran, president and CEO of Ovarian Cancer Research Alliance. “This collaboration allows OCRA to have a direct impact on future outcomes for our patients as well as add to the collective understanding of this disease.”

“We are excited to move forward in partnership with CRI, OCRA, and our collaborators with this important study. IPROC’s innovative trial design means that we can accelerate the pace of discovery in understanding how to optimize immunotherapy for the treatment of patients diagnosed with ovarian cancer,” said CCTG study lead Helen MacKay, MBChB, B.Sc., MRCP, M.D.

“Our hope is that the immunotherapy combinations we are studying in this clinical trial will do better than current standard-of-care treatments, providing ovarian cancer patients with much-needed therapeutic options and better odds of survival,” said Kunle Odunsi, M.D., Ph.D., FRCOG, FACOG, director of the University of Chicago Comprehensive Cancer Center and a study co-chair.

Key industry and academic partners

This clinical trial is the third to result from the collaboration formed in 2018 between CRI and CCTG, a Canada-based cooperative oncology group that

is sponsoring the study. AstraZeneca is collaborating to support this study. BioAtla, Inc., is supplying BA3011 and BA3021 as well as co-funding to support this study.

About the Trial

Title: Immunotherapy Platform Study in Platinum Resistant High Grade Serous Ovarian Cancer (IPROC) (NCT04918186)

Study Chairs:

- Helen MacKay, MBChB, B.Sc., MRCP, M.D., Head, Division of Medical Oncology and Hematology, Odette Cancer Center, Sunnybrook Health Sciences Centre, Toronto, ON Canada
- Kunle Odunsi, M.D., Ph.D., FRCOG, FACOG, Director, University of Chicago Comprehensive Cancer Center, Chicago, IL USA
- Anna Tinker, M.D., FRCPC, Medical Oncologist, British Columbia Cancer, Vancouver Centre, BC Canada
- Dmitriy Zamarin, M.D., Ph.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center, New York, NY USA

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About IMFINZI® (durvalumab)
AstraZeneca's IMFINZI is a human monoclonal antibody that binds to the PD-L1 protein and blocks the interaction of PD-L1 with PD-1 and CD80, countering the tumor's immune-evading tactics and releasing the inhibition of immune responses.

About Mecbotamab Vedotin (BA3011)
BioAtla's BA3011, CAB-AXL-ADC, is a conditionally and reversibly active antibody-drug conjugate targeting the receptor tyrosine kinase AXL that is overexpressed across multiple different solid tumors.

About Ozuriftamab Vedotin (BA3021)
BioAtla's BA3021, CAB-ROR2-ADC, is a conditionally and reversibly active antibody-drug conjugate directed against ROR2, a receptor tyrosine kinase that is overexpressed across many different solid tumors.

About the Cancer Research Institute
The Cancer Research Institute (CRI), established in 1953, is a highly rated U.S. nonprofit organization dedicated exclusively to saving more lives by fueling the discovery and development of powerful immunotherapies for all cancers. Guided by a world-renowned Scientific Advisory Council that includes four Nobel laureates and 27 members of the National Academy of Sciences, CRI has invested $474 million in support of research conducted by immunologists and tumor immunologists at the world's leading medical centers and universities and has contributed to many of the key scientific advances that demonstrate the potential for immunotherapy to change the face of cancer treatment. To learn more, go to cancerresearch.org and follow CRI on Twitter @CancerResearch.

About the CRI Anna-Maria Kellen Clinical Accelerator
CRI's clinical program, the Anna-Maria Kellen Clinical Accelerator is a unique academic-nonprofit-industry collaboration model that serves an as "incubator" that delivers multicenter clinical trials of promising new immunotherapy combinations. CRI's venture philanthropy fund supports clinical trials within the program, which fosters a collaborative environment that enables scientists to advance their most ambitious research ideas by accelerating studies that one group or company could not do alone. To learn more, go to cancerresearch.org/clinical-accelerator.

About Ovarian Cancer Research Alliance
Ovarian Cancer Research Alliance (OCRA) is the largest non-government funder of ovarian cancer research and has invested $110 million in research since its founding. OCRA fights ovarian cancer from all fronts, including in the lab and on Capitol Hill, and through innovative programs to support patients and their families.

OCRA's ongoing investments in the most promising scientific research is funding discoveries, creating new treatments, and hastening desperately needed breakthroughs. OCRA is *the* voice for the ovarian cancer community, working with legislators to ensure federal ovarian cancer research and education, patient safety, and access to high-quality care are protected on Capitol Hill. OCRA's programs help people navigate their diagnosis and support patients and their families when and where they need it most. Visit ocrahope.org to learn more

About Canadian Cancer Trials Group
The Canadian Cancer Trials Group (CCTG) is a cancer clinical trials research cooperative that runs phase I-III trials to test anti-cancer and supportive therapies at over 85 hospitals and cancer centers across Canada. From the operations center at Queen's University , CCTG has supported more than 600 trials enrolling 100,000 patients from 40 countries on 6 continents through a global network of 20,000 investigators and clinical trial staff. CCTG is a national program of the Canadian Cancer Society and their aim is to improve survival and quality of life for all people with cancer.

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