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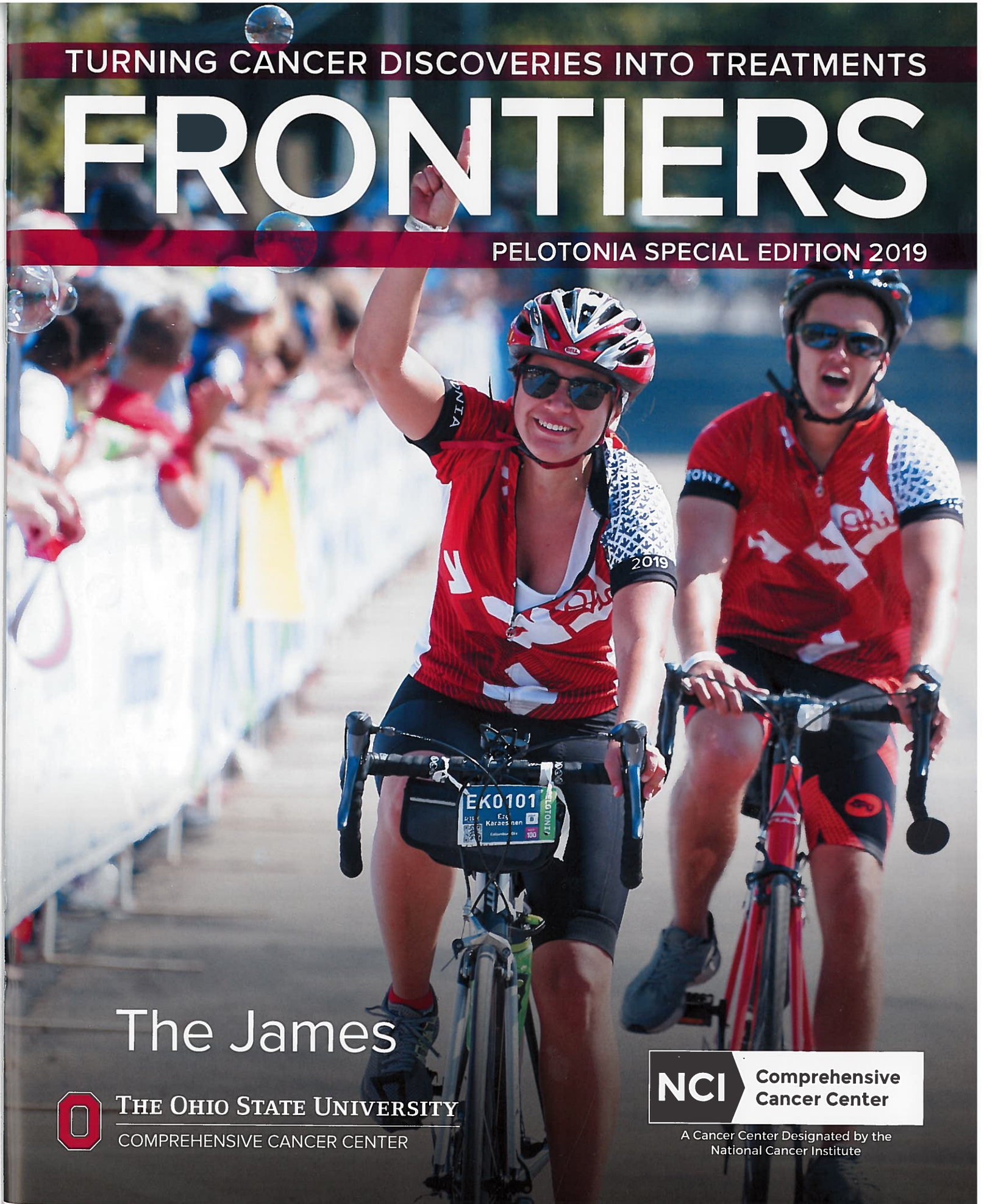


The James

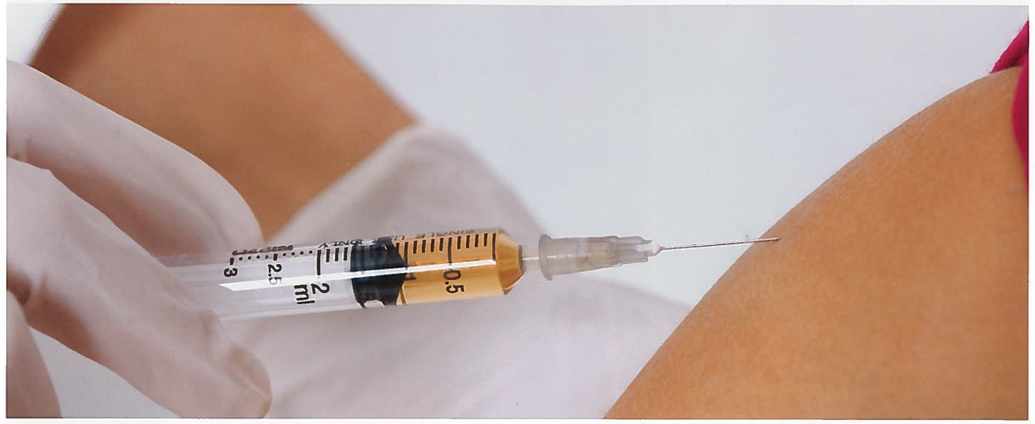
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

NCI Comprehensive Cancer Center

A Cancer Center Designated by the National Cancer Institute

Pelotonia Supports Clinical Trial Research at the OSUCCC – James

Novel Anticancer Vaccine Shows Promise in Phase I Study



Pravin Kaumaya, PhD

Promising results from an OSUCCC – James phase I clinical trial on a novel peptide vaccine suggest an important potential benefit of this vaccine and warrant its continuing development for treating patients with metastatic or recurrent solid tumors that overexpress the HER-2 protein.

Led by principal investigator **Pravin Kaumaya, PhD**, a professor in the Department of Obstetrics and Gynecology at Ohio State and member of the Translational Therapeutics Program at the OSUCCC – James, the trial demonstrates that the vaccine, called B-Vaxx, is well tolerated and can generate sustained anti-HER-2 immune response compared to humanized monoclonal antibodies, to which most patients develop resistance.

This study, which was supported in part by funding from Pelotonia and by grants from the National Cancer Institute, gave preliminary indication that peptide vaccination may help patients avoid therapeutic resistance and may offer a promising alternative to monoclonal antibody therapies such as Herceptin® and Perjeta®.

Reporting in the journal *Clinical Cancer Research*, Kaumaya and colleagues state that HER-2 is overexpressed in multiple epithelial tumors, including breast, gastro-esophageal, endometrial, ovarian, colorectal and lung cancers. They also note that HER-2 is associated with more aggressive forms of cancer, increased metastasis and decreased survival, making it a key therapeutic target in many malignancies.

The scientists describe B-Vaxx as a B-cell epitope-specific vaccine that combines two peptide B-cell epitope vaccines: measles virus fusion (MVF)-HER-2 corresponding to amino acid sequences 597-626 (pertuzumab), and MVF-HER-2 corresponding to amino acid sequences 266-296 (trastuzumab) incorporating a "promiscuous" MVF T-cell epitope. The two peptide constructs were conceived and designed by Kaumaya.

"Overall, immunotherapy using cancer vaccines is an exciting and rapidly evolving field in oncology that leverages patients' immune systems to target cancer," the scientists write in *Clinical Cancer Research*. "Chimeric B-cell epitope peptide vaccines incorporating a 'promiscuous' T-cell epitope offer an attractive immunotherapeutic option in the treatment of cancer."

The primary objectives of this first-in-human clinical trial, registered at Clinicaltrials.gov (NCT 01376505) and conducted under an investigational new drug application approved by the U.S. Food and Drug Administration, were to assess the safety and toxicity of immunization, determine the optimum immunologic/biologic dose of the new combination HER-2 vaccine, measure humoral and cellular immune responses, and evaluate therapeutic benefit.

The trial, which took place entirely at Ohio State, involved 49 patients with metastatic or recurrent tumors and a median of four prior lines of chemotherapy who received at least one inoculation of B-Vaxx. Of these, 28 patients received three or more vaccinations. Two of these showed a partial response and 14 exhibited stable disease.

"The vaccine generated sustained humoral response-eliciting HER-2-specific antibodies in the majority of responding patients," the scientists write, adding that most patients had minimal or no toxicities, and no dose-limiting toxicities were observed.

The scientists' report addresses a few limitations of the clinical trial, such as it being a single-institution study involving a heterogeneous group of cancer patients who were heavily pre-treated. "Such patients tend to have poor ability to mount an effective antitumor immunity because of tumor- and treatment-induced immunosuppression," they explain, adding that patients who are less heavily pretreated or have a lower tumor burden stage a more effective and sustained immune response.

They go on to state that the trial suffered from a lack of randomization and from an absence of consistent measurement of HER-2 overexpression in patients enrolled in the dose-escalation part of the study. "This is partly because the phase I trial was open to all patients irrespective of whether they overexpressed HER-2."

Overall, the scientists conclude that, in addition to being well tolerated and able to generate sustained anti-HER-2 immune response, the vaccine induced patient antibodies that showed potent antitumor activity.

Given the successful phase I trial results, Kaumaya says, "Continuous development of the vaccine is ongoing at the OSUCCC – James in a phase II trial at the suggested optimum biological dose in a less heavily pretreated patient population in breast and/or gastrointestinal malignancies with HER-2/EGFR overexpression." This trial is supported by funds from within the Comprehensive Cancer Center.

Kaumaya is PI for this trial, and **Robert Wesolowski, MD**, of the Division of Medical Oncology at Ohio State, is clinical PI. Kaumaya says 12 patients are being accrued to the study, and an expansion cohort of 36 patients is planned. "These studies should allow a sustained humoral response to the vaccine, potentially resulting in a greater observed clinical benefit," he adds.

Kaumaya, who directs the Peptide and Protein Engineering Laboratory within the OSUCCC – James and Ohio State's College of Medicine, says other promising work comprising vaccines developed for HER-1, HER-3, IGF-1R and VEGF at the university has been licensed to IMUGENE Limited, an Australian-based biotechnology company that develops cancer immune-therapies targeting B-cell peptide vaccines. This work, he adds,

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demonstrates a growing immune-oncology platform for developing combination immunotherapy, widely considered the next frontier in treating cancer.

For example, his team recently developed a PD-1-Vaxx (programmed cell death) B-cell peptide cancer vaccine that induces the body to produce polyclonal antibodies that block PD-1 signaling and produce an anticancer effect similar to the marketed immunotherapy drugs Keytruda® and Opdivo®.

"PD-1-Vaxx has shown great potential in preclinical studies that we presented at the 2019 annual meeting of the American Association for Cancer Research," Kaumaya says. "It outperformed an industry-standard mouse anti-PD-1 antibody in a syngeneic mouse model of HER2+ colorectal cancer. When we used it in combination with our B-Vaxx vaccine, it inhibited tumor growth in a colon carcinoma model challenged with CT26/HER-2 cell line."

Kaumaya says a phase 1b human clinical trial with the new PD-1 vaccine is being planned for this fall at Ohio State and the Mayo Clinic. Kaumaya also is devising peptide vaccines for the PD-L1, TIM3 and Lag-3 targets, which will be developed as combination immunotherapy.