CRI Cancer Research Institute™

2025 CRI INVESTIGATORS

Clinical Innovator Award

CRI Clinical Innovator Award

The Cancer Research Institute (CRI) Clinical Innovator Award supports bold, early-phase immunotherapy clinical trials that address some of the most pressing challenges in cancer treatment. These investigator-initiated trials explore novel therapeutic approaches and seek to uncover the biological mechanisms driving patient response, advancing both treatment innovation and biomarker discovery to help predict which patients are most likely to benefit.

CRI Clinical Innovator studies are selected through a rigorous, expert-driven review process that emphasizes scientific merit, patient impact, and unmet medical need. Awarded investigators receive scientific guidance from CRI focused on maximizing translational impact. To date, CRI has supported nine clinical trials across Australia, Italy, Spain, and the U.S. New awards of $1 million are made annually, with over $8.5 million invested to date.

By advancing innovative, high-impact trials, the Clinical Innovator Award accelerates the development of more precise and effective cancer immunotherapies. These studies represent more than clinical research – they are opportunities to shift treatment paradigms and improve outcomes for patients who need better options now.

A Letter from Our CEO

At CRI, we fund ideas that can change the way cancer is treated by harnessing the power of the body's own immune system – and the following clinical trials exemplify that mission.

Through our Clinical Innovator Award, CRI supports early-phase immunotherapy clinical trials that ask big, urgent questions:

- Can we intercept cancer before it starts?
- Can we make treatment more precise, more durable, and more accessible?
- Can we finally unlock immunotherapy's full potential in cancers that have long resisted it?

These trials represent the future of cancer care. Each one is designed not only to test a novel therapeutic strategy but also to uncover the biological insights that explain why treatments work – or why they don't. Embedded within these studies is the pursuit of predictive biomarkers, a deeper understanding of the tumor microenvironment, and a drive to personalize treatment for patients in need of new hope or for those left behind by conventional cancer care.

This year's Clinical Innovator portfolio includes efforts to improve survival rates in pancreatic cancer, develop a scalable vaccine for bladder cancer, and prevent oral lesions from becoming cancer. These trials span continents and organizations, but they are united by a common thread: bold science with the potential to transform outcomes.

We are proud to support these studies and even more excited about where they might lead.

With gratitude,

Alicia Zhou, PhD
Chief Executive Officer
Cancer Research Institute

Randomized phase 1b trial of shared FGFR3 neoantigen peptide vaccine in combination with TAR-210 or TAR-210 monotherapy for FGFR3-mutated intermediate-risk non-muscle invasive bladder cancer

Research Focus: Bladder cancer, cancer vaccines, genetic mutations

Principal Investigator

Nina Bhardwaj, MD, PhD

Co-Investigators

Jonathan Anker, MD, PhD
Mesude Bicak, PhD
Marcio Diniz, PhD
Matthew Galsky, MD
Mansi Saxena, PhD
John Sfakianos, MD

Clinical Trial Site

Icahn School of Medicine at Mount Sinai

Cancer is driven by genetic mutations that cause uncontrolled cell growth. Immunotherapies like neoantigen vaccines take advantage of these mutations to trigger targeted immune responses with fewer side effects. While this approach holds great promise, developing a personalized vaccine for every patient is costly and time- and labor- intensive. Dr. Nina Bhardwaj and colleagues are exploring a more practical solution: an "off-the-shelf" vaccine that targets mutations commonly shared across many patients.

Non-muscle invasive bladder cancer (NMIBC) accounts for 75-80% of all newly diagnosed bladder cancers, and patients with intermediate- or high-risk NMIBC face high rates of recurrence and disease progression. Most intermediate-risk patients have mutations in the *FGFR3* gene, making it an ideal target for a shared vaccine approach. Prior studies have shown that *FGFR3* mutations can stimulate anti-tumor immune responses and that vaccines targeting these mutations can produce both clinical and immunologic benefits.

This new clinical trial will evaluate two different FGFR3-targeted treatment strategies for patients with intermediate-risk NMIBC: 1) a vaccine targeting *FGFR3* mutations and 2) a novel slow-release bladder-inserted device (TAR-210) that delivers an FGFR3 inhibitor directly to the tumor. Patients will receive either TAR-210 alone or TAR-210 plus the vaccine to determine whether the combination improves outcomes. This innovative study aims to make targeted immunotherapy more accessible, durable, and scalable for patients with bladder cancer.

> "Cancer vaccines represent a promising approach to provide long-lasting clinical benefit with limited side effects.

Immunotherapy for the prevention of high-risk oral disorders malignant transformation - The APHRODITE Trial

Research Focus: Oral cavity cancer, cancer prevention, microbiome

Principal Investigator

Paolo Bossi, MD

Co-Investigators

Luigi Lorini, MD
Enrico Lugli, PhD
Giuseppe Mercante, MD
Alberto Paderno, MD, PhD
Maria Rescigno, PhD

Clinical Trial Sites

IRCCS Humanitas Research Hospital
ASST Santi Paolo e Carlo
European Institute of Oncology
ASST Sette Laghi
ASST Lariana
Federico II University
University of Bologna

Some mouth lesions, known as oral potentially malignant disorders (OPMDs), carry a significant risk of becoming cancerous – ranging from 1% to nearly 50%. Even after surgical removal, many of these lesions can still progress to cancer. Dr. Paolo Bossi and colleagues will test a new immunotherapy-based approach to stop that transformation before it happens.

The APHRODITE Trial focuses on mitazalimab, an immune-stimulating, "orphan" drug that activates a pathway called CD40, which plays a key role in immune surveillance and tumor prevention. In this phase II trial, patients with high-risk OPMDs will receive mitazalimab over an eight-week period. After six months, the team will assess whether the treatment reduced or eliminated abnormal tissue and, evaluate its safety, impact on cancer risk, and effects on quality of life.

The study will also analyze blood, tissue, and saliva samples to understand how the immune system and microbiome respond to treatment, insights that could help identify which patients are most likely to benefit. If successful, this approach could offer a less invasive, immunotherapy-based alternative to surgery and, transform care for patients with pre-cancerous oral lesions.

> "This work is part of a growing field known as 'cancer interception', which aims to stop cancer before it starts and improve long-term outcomes.

Randomized phase II study of neoadjuvant NALIRIFOX with and without PD1 and CXCR4 inhibition for potentially resectable pancreatic cancer

Research Focus: Pancreatic cancer, tumor microenvironment, neoadjuvant therapy

Principal Investigator

Rachael Safyan, MD

Co-Investigators

E. Gabriela Chiorean, MD
Venu Pillarisetty, MD

Clinical Trial Sites

University of Washington
Fred Hutchinson Cancer Center
University of Cincinnati

Pancreatic cancer is one of the most aggressive and deadly cancers, with less than 15% of patients surviving five years after diagnosis. Even when tumors appear operable, many patients relapse after surgery and chemotherapy. Drs. Rachael Safyan, E. Gabriela Chiorean, and Venu Pillarisetty aim to improve those odds by testing whether adding immunotherapy to current gold standard treatment can increase the chances of a cure.

To date, few immunotherapies have been effective in patients with pancreatic cancer, in part because these tumors are especially skilled at evading the immune system by forming a barrier that keeps immune cells out. But, two immunotherapy drugs – cemiplimab (Libtayo®), which is approved to treat patients with basal cell carcinoma and cutaneous squamous cell carcinoma, and motixafortide (Aphexda®), which is approved to treat patients with multiple myeloma – may help break through that wall.

This new clinical trial will test these two drugs in combination with a chemotherapy regimen called nalirifox (liposomal irinotecan [Onivyde®], 5 fluorouracil/leucovorin, and oxaliplatin) given before surgery. The goal is to shrink tumors, improve surgical outcomes, and prevent relapse. This study represents a critical step toward making immunotherapy effective in one of cancer's most difficult frontiers.

> "If successful, this study could lead to a new standard of care and bring curative treatment within reach for more patients facing pancreatic cancer.

About CRI

The Cancer Research Institute (CRI) is a nonprofit organization dedicated to advancing the field of cancer immunotherapy through rigorous scientific research and global collaboration. Since 1953, CRI has been instrumental in uncovering the fundamental biology of the immune system and its application to cancer treatment, laying the groundwork for breakthroughs such as checkpoint blockade, cancer vaccines, and engineered cell therapies.

CRI's mission is to create a world immune to cancer by driving scientific discovery, accelerating collaboration, and turning breakthroughs into life-saving treatments. Our work bridges the gap between discovery and patient impact, ensuring that scientific innovation translates into real-world treatments.

To date, CRI has committed over $560 million to research impacting more than 30 cancer types. Our funding strategy is built on the framework of People × Biology × Data: supporting world-class scientists, deepening understanding of tumor-immune system interactions, and harnessing data to guide discovery and translation. By uniting these elements, CRI catalyzes innovation through our global research ecosystem to drive the next generation of discoveries forward.

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