Weill Cornell Medicine

Why Aren’t We Immune to Prostate Cancer ?

ZERO Prostate Cancer – 11/19/2026

Jedd Wolchok, MD, PhD
Meyer Director, Meyer Cancer Center

November 1, 2025

We’re Changing Medicine.

How Might We Prevent Or Even Cure Cancer?



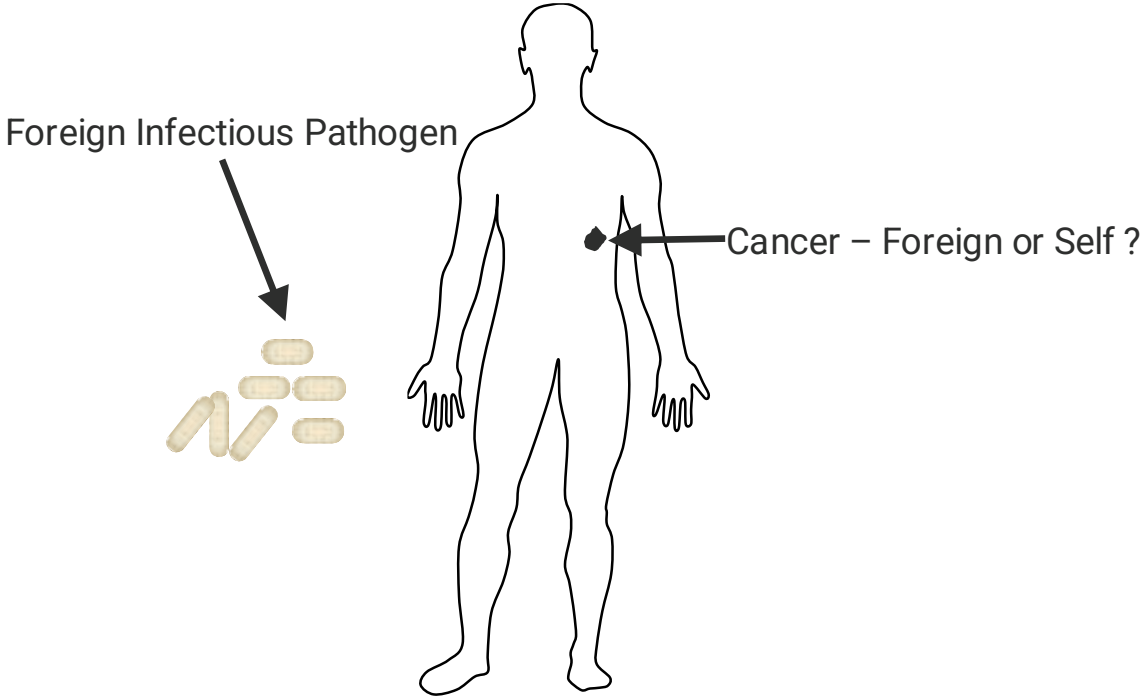
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NewYork-Presbyterian

Is there an immune response to cancer?

Can the immune system reject cancer?

Cancer: Is it self or non-self?



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Development of immunotherapy has been a long journey

1892

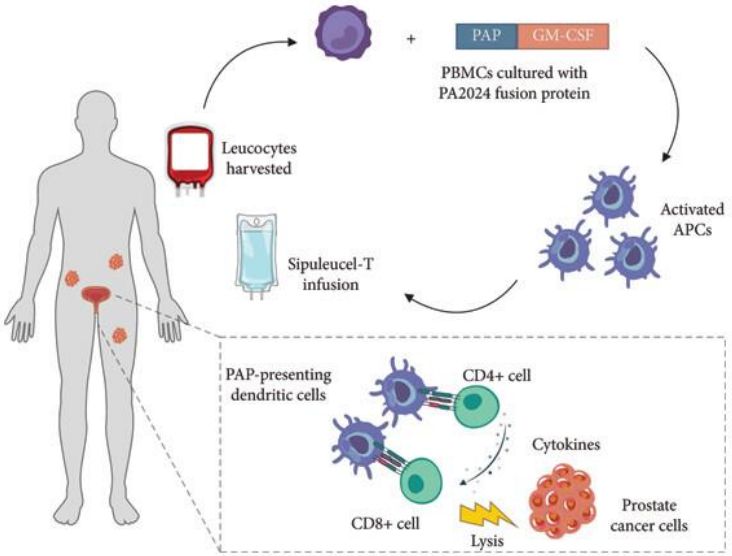


2013



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Cellular Immunotherapy for Prostate Cancer: Lessons Learned From 15 Years of Sipuleucel-T



Prostate Cancer, Volume: 2025, Issue: 1, First published: 31 December 2025, DOI: (10.1155/proc/9766669)

‘Driving’ An Immune Response



T-cell receptor:
Antigen-MHC



CD28:B7



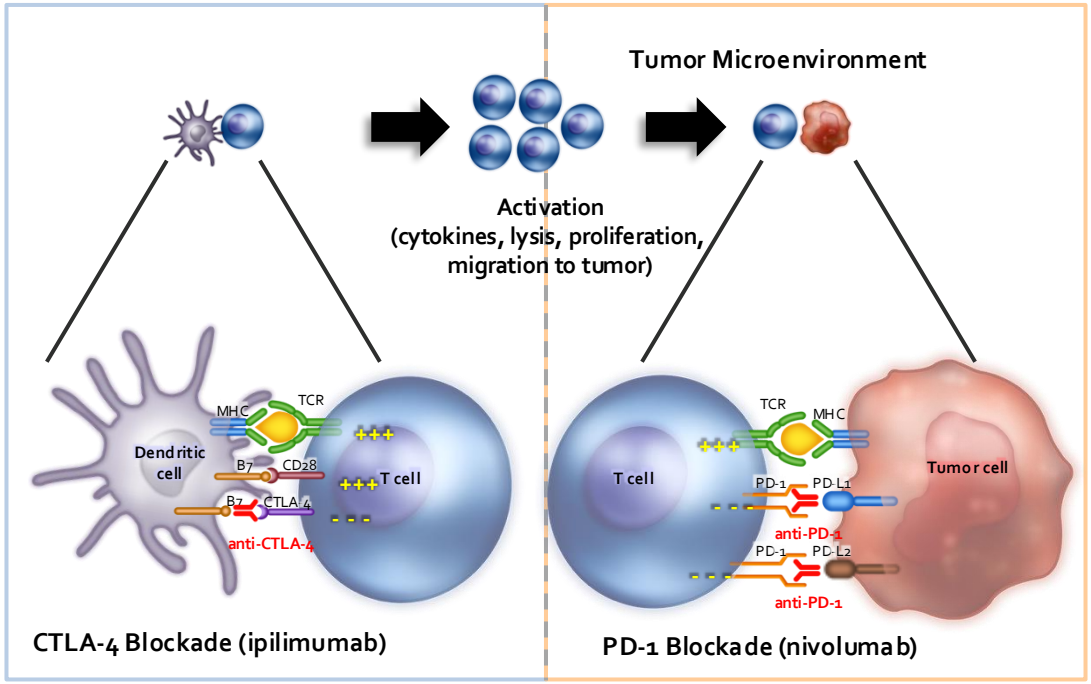
CTLA-4: B7



Vaccine?

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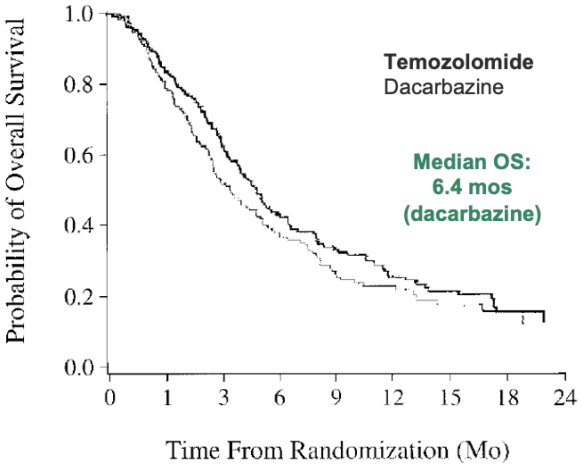
Blocking the Immune Brakes: CTLA-4 and PD-1



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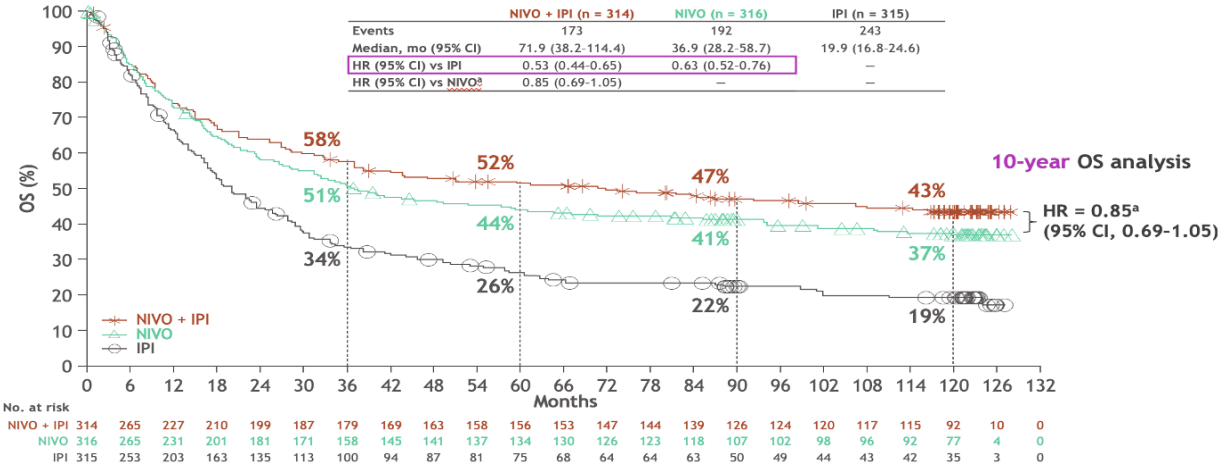
Expectations for Overall Survival in Metastatic Melanoma With Immunotherapy: 2000-2025

Pre-Checkpoint Blockade/ BRAF-Targeted Therapy: Chemotherapy



(Middleton MR et al. *J Clin Oncol* 2000)

PD-1 +/- CTLA-4 Inhibition



(Wolchok et al. *New Eng J Med* 2025)

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IMMUNE-MEDIATED ADVERSE REACTIONS

Follow color code to appropriate management guide section.

GASTROINTESTINAL

GO TO PAGE 6

Signs and symptoms such as

- Diarrhea
- Abdominal pain
- Blood or mucus in stool
- Bowel perforation
- Peritoneal signs
- Ileus

LIVER

GO TO PAGE 8

Signs such as

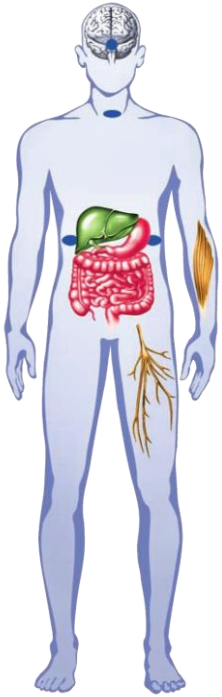
- Abnormal liver function tests (eg, AST, ALT) or total bilirubin

SKIN

GO TO PAGE 10

Symptoms such as

- Pruritus
- Rash



NEUROLOGIC

GO TO PAGE 12

Symptoms such as

- Unilateral or bilateral weakness
- Sensory alterations
- Paresthesia

ENDOCRINE

GO TO PAGE 14

Signs and symptoms such as

- Fatigue
- Headache
- Mental status changes
- Abdominal pain
- Unusual bowel habits
- Hypotension
- Abnormal thyroid function tests and/or serum chemistries

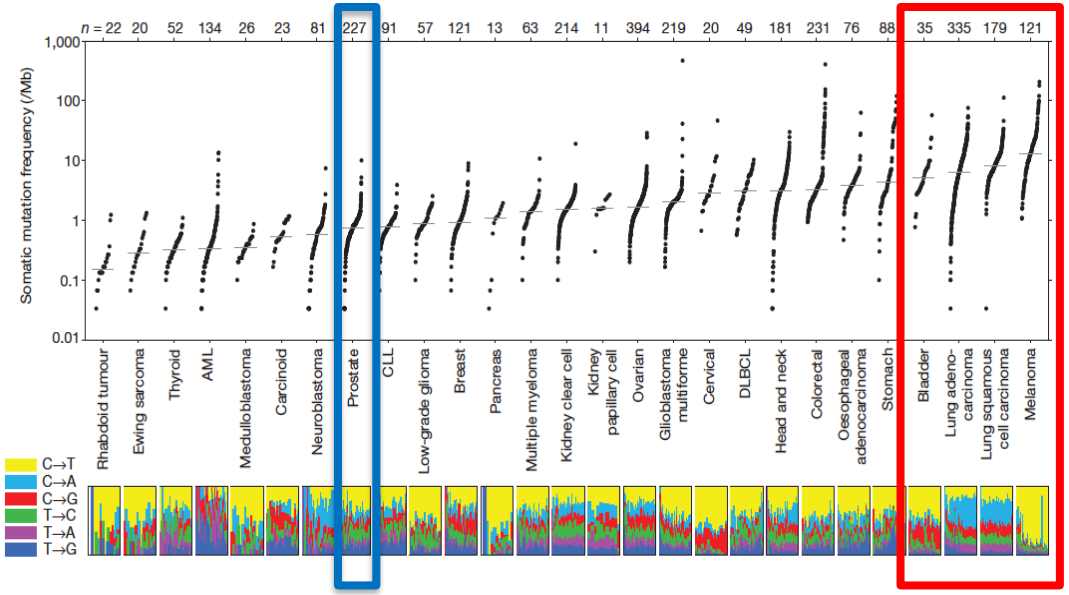
OTHER ADVERSE REACTIONS, including ocular manifestations

GO TO PAGE 16

Please see each organ system section for related guidance.

- Result from increased or excessive immune activity
- Can be severe or life-threatening, affecting various organs

Genomics may explain why some cancers respond to immunotherapy

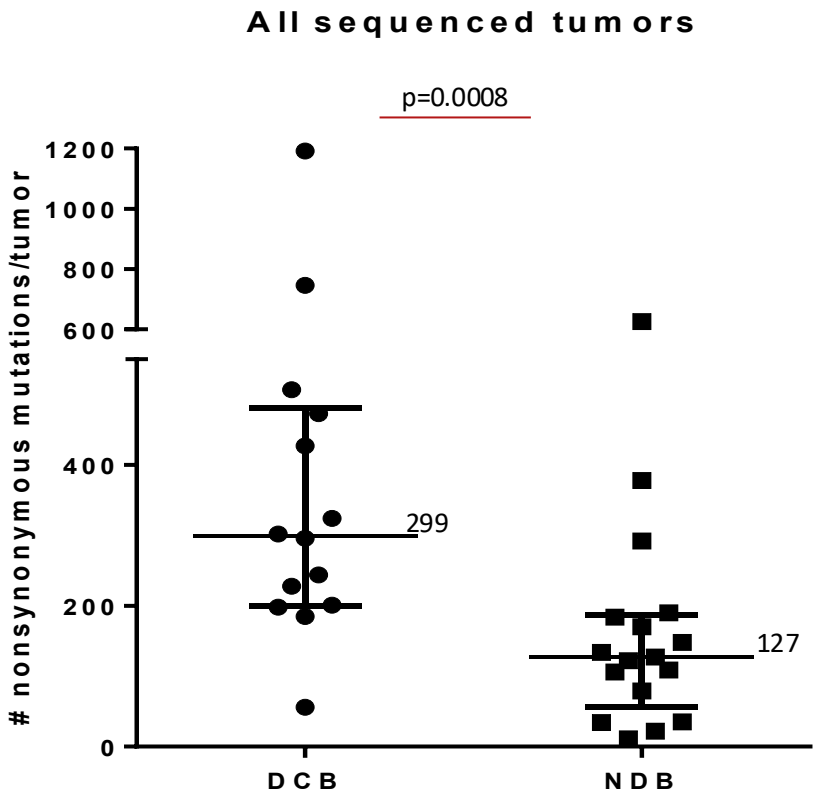


Lawrence *et al*, *Nature* 2013

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Number of mutations in lung cancer tumors correlates with clinical outcome from immunotherapy

Hypothesis: More mutations makes a tumor look less like 'Self' to the immune system, increasing immune interest in tumor



Rizvi, Hellmann, Snyder *et al*, *Science* 2015

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Ipilimumab versus placebo after radiotherapy in patients with metastatic castration-resistant prostate cancer that had progressed after docetaxel chemotherapy (CA184-043): a multicentre, randomised, double-blind, phase 3 trial

*Eugene D Kwon, Charles G Drake, Howard I Scher, Karim Fizazi, Alberto Bossi, Alfons J M van den Eertwegh, Michael Krainer, Nadine Houede, Ricardo Santos, Hakim Mahammedi, Siobhan Ng, Michele Maio, Fabio A Franke, Santhanam Sundar, Neeraj Agarwal, Andries M Bergman, Tudor E Ciuleanu, Ernesto Korbenfeld, Lisa Sengeløv, Steinbjorn Hansen, Christopher Logothetis, Tomasz M Beer, M Brent McHenry, Paul Gagnier, David Liu, Winald R Gerritsen, for the CA184-043 Investigators**

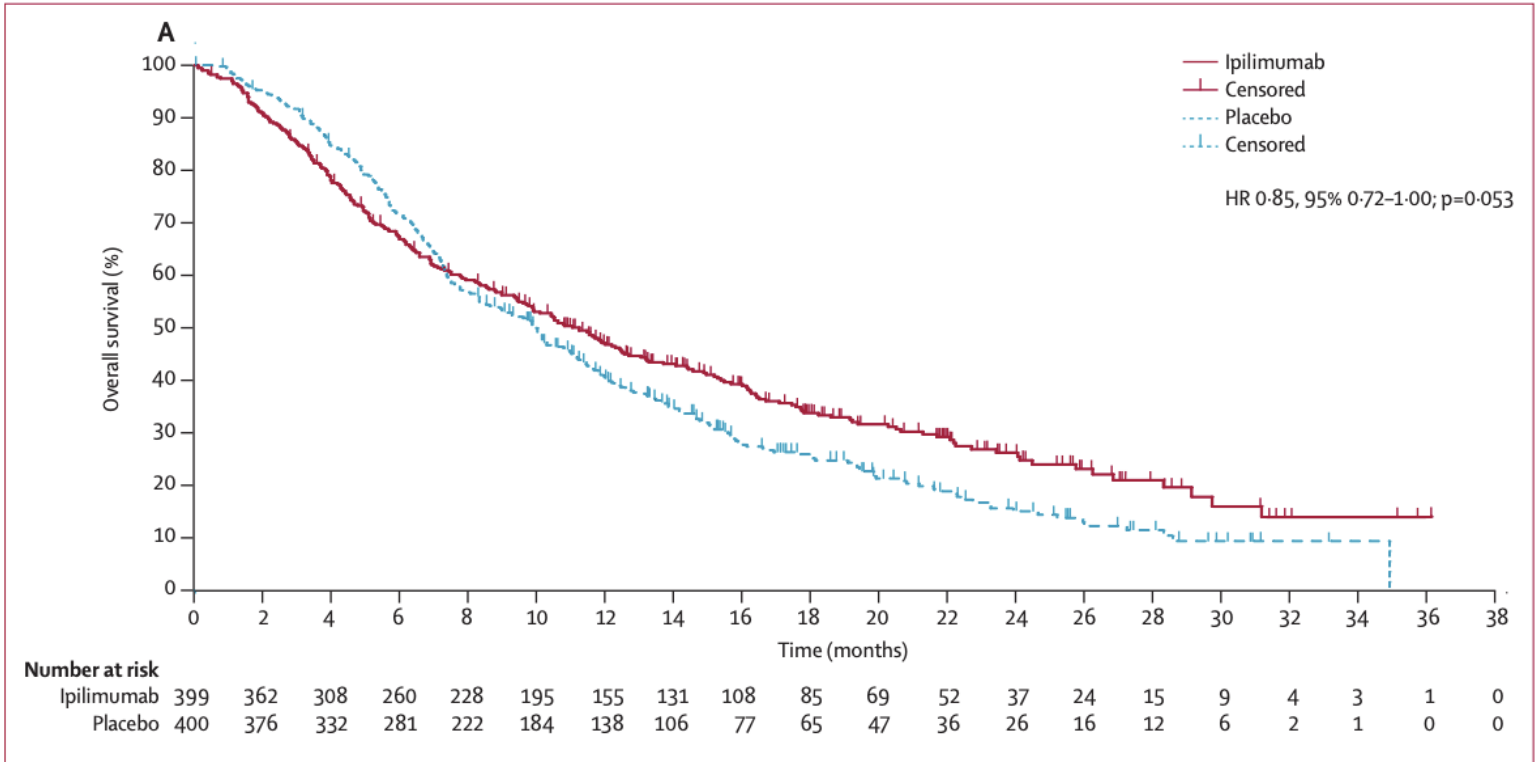
Lancet Oncol 2014; 15: 700–12

Published Online
May 13, 2014
http://dx.doi.org/10.1016/

Summary

Background Ipilimumab is a fully human monoclonal antibody that binds cytotoxic T-lymphocyte antigen 4 to enhance antitumour immunity. Our aim was to assess the use of ipilimumab after radiotherapy in patients with metastatic castration-resistant prostate cancer that progressed after docetaxel chemotherapy.

Overall survival: a ‘near miss’



Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

ORIGINAL REPORTS | November 27, 2019

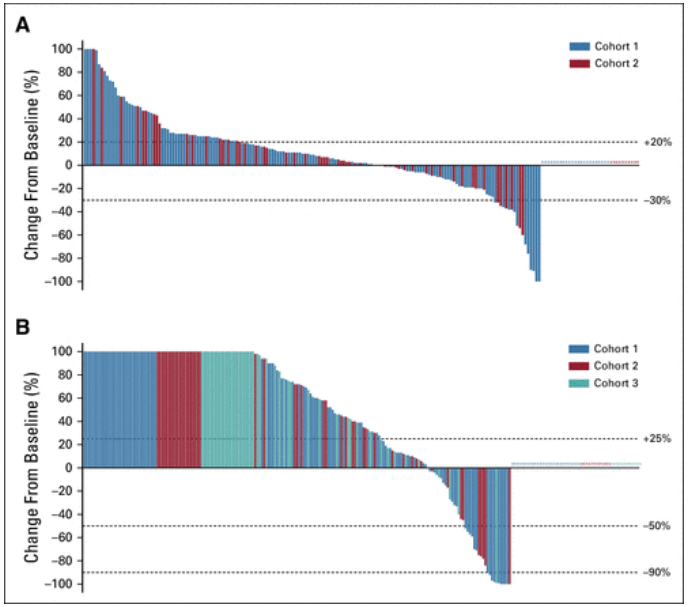
Pembrolizumab for Treatment-Refractory Metastatic Castration-Resistant Prostate Cancer: Multicohort, Open-Label Phase II KEYNOTE-199 Study

Authors: Emmanuel S. Antonarakis, MD, Josep M. Piulats, MD, PhD, Marine Gross-Goupil, MD, PhD, Jeffrey Goh, MBBS, Kristiina Ojamaa, MD, Christopher J. Hoimes, DO, Ulka Vaishampayan, MD, ... SHOW ALL ... , and Johann Sebastian de Bono, MD, PhD | AUTHORS INFO & AFFILIATIONS

J Clin Oncol **38**, 395-405(2020) • Volume 38, Number 5 • DOI: 10.1200/JCO.19.01638

23,666 / 689 Altmetric 328

PDF



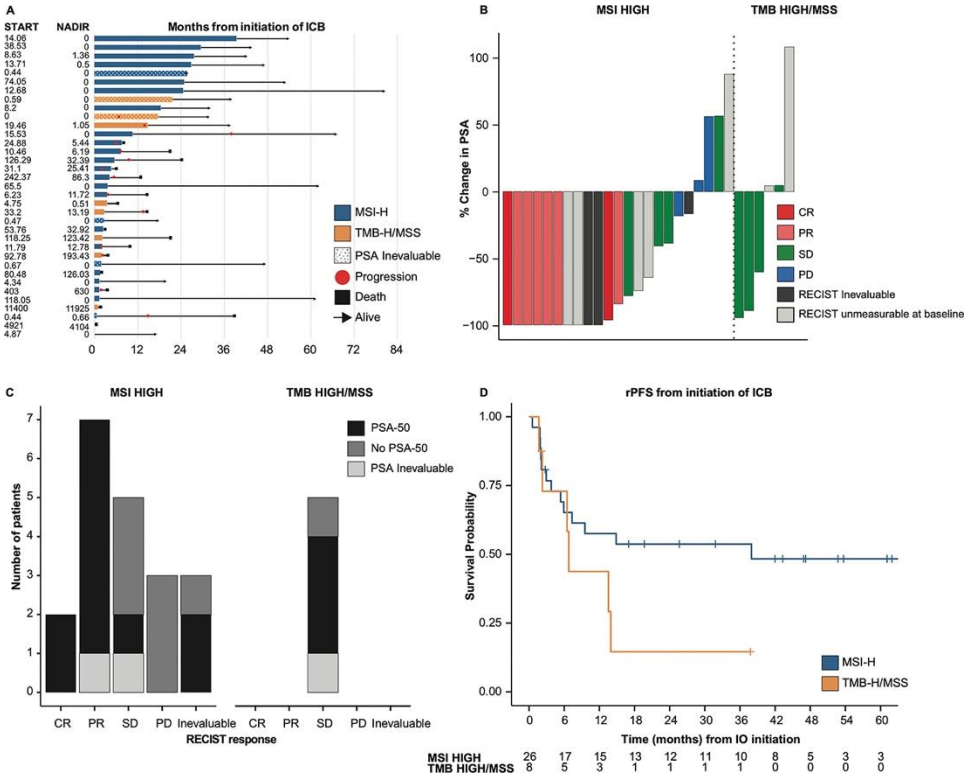
Imaging Response

PSA Response

FIG 2. Waterfall plots of change from baseline in tumor size and prostate-specific antigen (PSA) level. (A) Best percentage change from baseline in the sum of longest diameters of target lesions as assessed by RECIST v1.1 by central review in the 199 patients enrolled in cohorts 1 and 2. Asterisks represent the 23 patients in cohort 1 and 10 patients in cohort 2 who were not evaluable for change from baseline in tumor size because they did not have one or more evaluable postbaseline imaging assessment. (B) Best percentage change from baseline in PSA level in the 243 patients enrolled in cohorts 1, 2, and 3 who had a baseline PSA measurement. Asterisks represent the 27 patients in cohort 1, 12 patients in cohort 2, and 11 patients in cohort 3 who had a baseline PSA measurement but did not have one or more postbaseline PSA measurement. Changes > +100% were truncated at +100%.

Published in: Emmanuel S. Antonarakis; Josep M. Piulats; Marine Gross-Goupil; Jeffrey Goh; Kristiina Ojamaa; Christopher J. Hoimes; Ulka Vaishampayan; Ranaan Berger; Ahmet Sezer; Tuomo Alanko; Ronald de Wit; Chunde Li; Aurelius Omlin; Giuseppe Procopio; Satoshi Fukasawa; Ken-ichi Tabata; Se Hoon Park; Susan Feyerabend; Charles G. Drake; Haiyan Wu; Ping Qiu; Jeri Kim; Christian Poehlein; Johann Sebastian de Bono J Clin Oncol 2019 11-27
DOI: 10.1200/JCO.19.01638
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Response to pembrolizumab in prostate cancer patients with specific genomic features

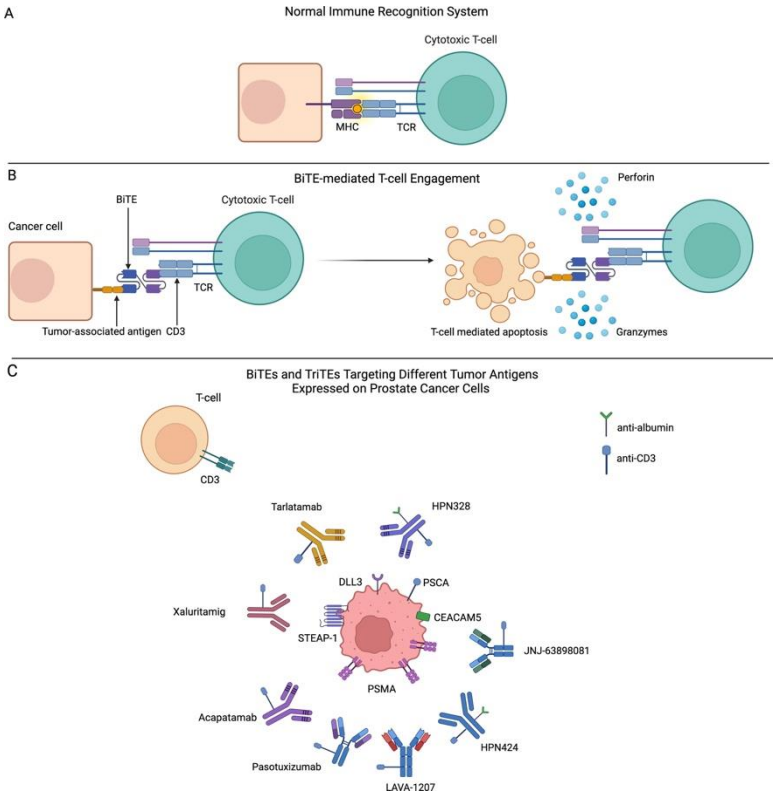


Lenis et al., *Clin Cancer Res*, 2024

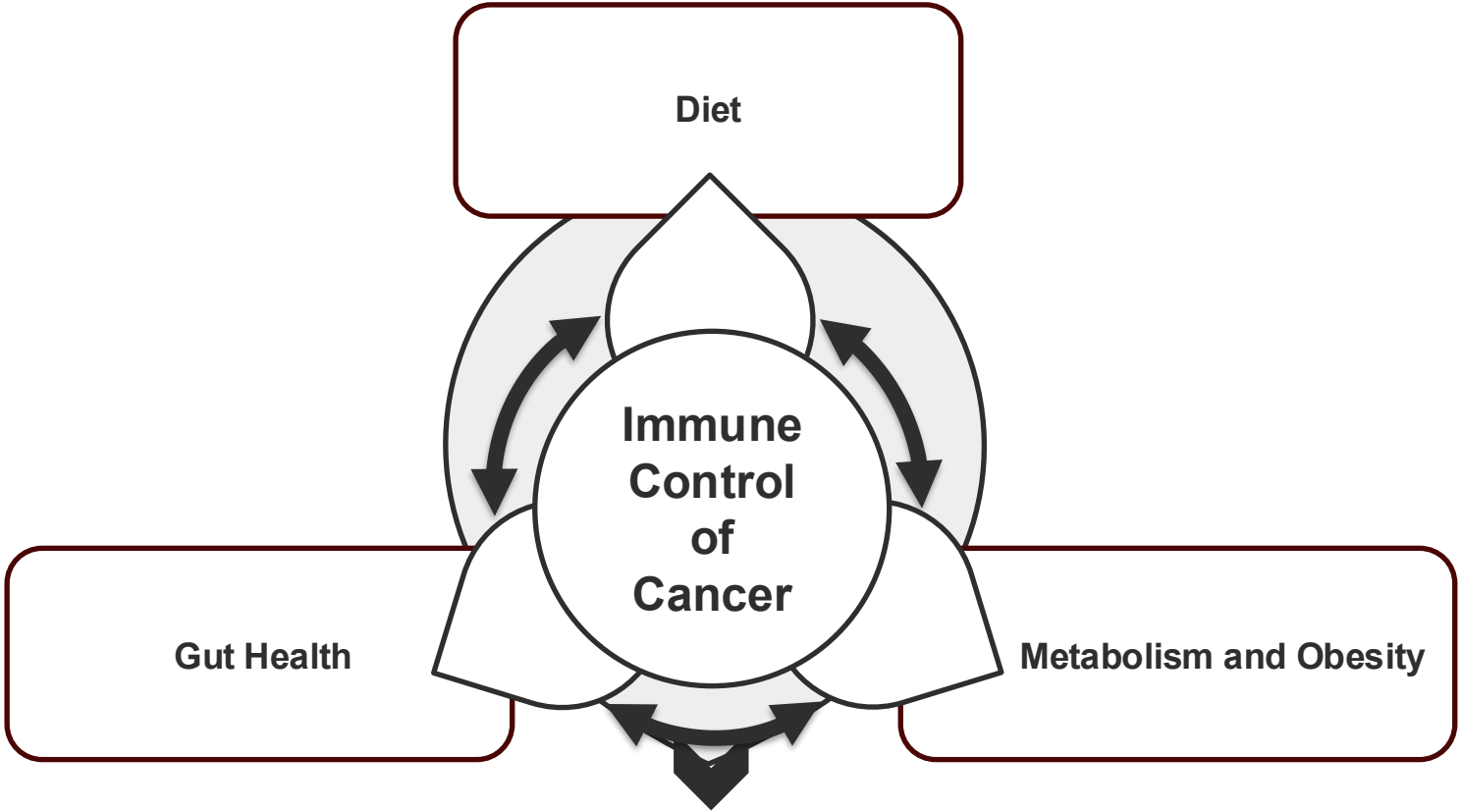
T-cell Engagers in Prostate Cancer

Chadi Hage Chehade, Zeynep Irem Ozay, Micah Ostrowski, Chiara Mercinelli, Georges Gebrael, Nicolas Sayegh, Umang Swami, Arun A. Azad, Emmanuel S. Antonarakis, Neeraj Agarwal

European Urology
Volume 87 Issue 5 Pages 553-558 (May 2025)
DOI: 10.1016/j.eururo.2025.02.001


A
Normal Immune Recognition System
Cytotoxic T-cell
MHC
TCR
B
BiTE-mediated T-cell Engagement
Perforin
BiTE
Cytotoxic T-cell
Cancer cell
TCR
Tumor-associated antigen
CD3
T-cell mediated apoptosis
Granzymes
C
BiTEs and TriTEs Targeting Different Tumor Antigens
Expressed on Prostate Cancer Cells
T-cell
CD3
anti-albumin
anti-CD3
Tarlatamab
HPN328
DLL3
PSCA
Xaluritamig
CEACAM5
STEAP-1
JNJ-63898081
PSMA
Acapatamab
HPN424
Pasotuxizumab
LAVA-1207

Can What You Eat and How You Process It Affect Cancer Treatment?



Novel Therapeutic Interventions



Weill Cornell Medicine

We're Changing Medicine.

The Weill Cancer Hub East

Revolutionizing Cancer Research for Therapeutic Breakthroughs

Uniting Expertise. Accelerating Discoveries. Transforming Care.

The Weill Cancer Hub East brings together the brightest minds from **Princeton University**, **The Rockefeller University**, **Weill Cornell Medicine** and **The Ludwig Institute** in a shared mission: to accelerate discoveries, advance therapies and bring new hope to cancer patients worldwide.

Thanks to groundbreaking discoveries in the study of immunotherapy, metabolism and the microbiome, we now have an unprecedented opportunity to reshape how we treat and prevent cancer. Using the latest findings in nutrition, immunology, computational analysis and artificial intelligence, this pioneering alliance will seek to define the complex relationship between solid tumors and the environment in which they form and grow.

By uniting basic, clinical and translational scientists from each of these world-class institutions, the Weill Cancer Hub East will leverage their collective expertise, harness their complementary strengths and employ cutting-edge technology in order to revolutionize cancer research.

Princeton University is renowned for its study of cancer metabolism, including basic cancer research, metabolomics, genomics, biology, and the computational and physical sciences, discovering new and better ways to prevent and treat cancer through nutrition and medication.

PRINCETON UNIVERSITY

Rockefeller University, the world's leading biomedical research university, is singularly focused on powering the breakthroughs that will transform medicine. Their cancer researchers are unlocking the mysteries of cancer metastasis and gene regulation and developing the next generation of cancer therapeutics that selectively target metastatic disease.

The Rockefeller University

Weill Cornell Medicine is a leader in immunotherapy and cancer care, serving a diverse patient population across New York City. With world-class physicians and pioneering scientists, Weill Cornell Medicine and the Sandra and Edward Meyer Cancer Center are dedicated to accelerating personalized translational medicine and transforming cancer care through groundbreaking discoveries that improve patient outcomes.

Weill Cornell Medicine

LUDWIG CANCER RESEARCH

The Ludwig Institute for Cancer Research is an international nonprofit organization at the forefront of cancer research, providing its broad network of scientists with vital resources to advance life-changing discoveries for the prevention, diagnosis and treatment of cancer. Ludwig scientists are leaders in fields such as tumor immunology, tumor biology, the tumor microenvironment and cancer metabolism.

The Weill Cancer Hub East

Transforming Cancer Care with Cutting-Edge Science

Harnessing Nutrition and Metabolism to Control Cancer

Researchers at the Weill Cancer Hub East are working to unravel the complex interplay of immunity, metabolism and the microbiome. Cancer is a highly dynamic disease, shaped not only by genetic mutations but also by the metabolic and immune environments in which it develops.



The Promise and Complexity of Immunotherapy

Immunotherapy, a powerful approach to many types of cancer, is heralded as the "fifth pillar" alongside surgery, radiation, chemotherapy and precision-targeted therapeutics. Unlike traditional treatments that attack cancer cells directly, immunotherapy empowers a patient's own immune system to strike the disease from within. Despite its immense promise, the effectiveness of immunotherapy varies greatly from cancer to cancer, person to person, and clinicians and scientists are seeking answers.

Enhancing Treatment Efficacy Through Metabolic Science

Hub scientists will use advanced technology to study how diet and the microbes that metabolize our food influence our cells and enhance the immune response to cancer. Emerging research spotlights the crucial roles of metabolic reprogramming and gut microbiota in shaping anti-tumor immunity and response to therapy. The Hub's researchers aim to systematically decode these interactions to enhance treatment efficacy.

Key Research Areas

The Weill Cancer Hub East aims to bridge fundamental discoveries with clinical applications, **translating insights from bench to bedside** to develop more effective, personalized cancer therapies.

Precision Strategies for Targeting Tumors

- **Computational Genomics & Tumor Targets** – Identifying tumor vulnerabilities, analyzing treatment resistance, and uncovering new therapeutic targets through advanced computational methods
- **Tumor Microenvironment & Immunotherapy** – Investigating how tumors suppress immune responses and developing strategies to overcome these barriers, improving immunotherapy effectiveness
- **Cell Therapy for Solid Tumors** – Enhancing immune cell therapies by overcoming metabolic challenges and optimizing their function in solid tumors



Metabolism & Cancer: Unlocking New Therapeutic Pathways

- **Microbiome & Tumor Inflammation** – Exploring how gut microbiota influence tumor growth, immune response, and immunotherapy success to improve treatment outcomes
- **Lipid Metabolism & Cancer** – Examining how obesity-driven lipid metabolism fuels cancer progression and identifying new therapeutic targets
- **Diet & Cancer Metabolism** – Investigating diet's role in cancer progression and immune response to develop innovative strategies for prevention and treatment

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