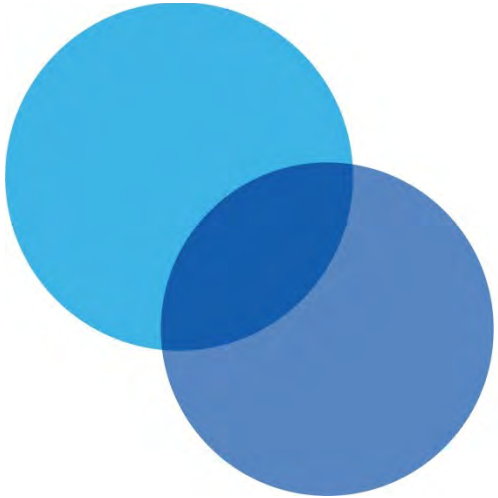


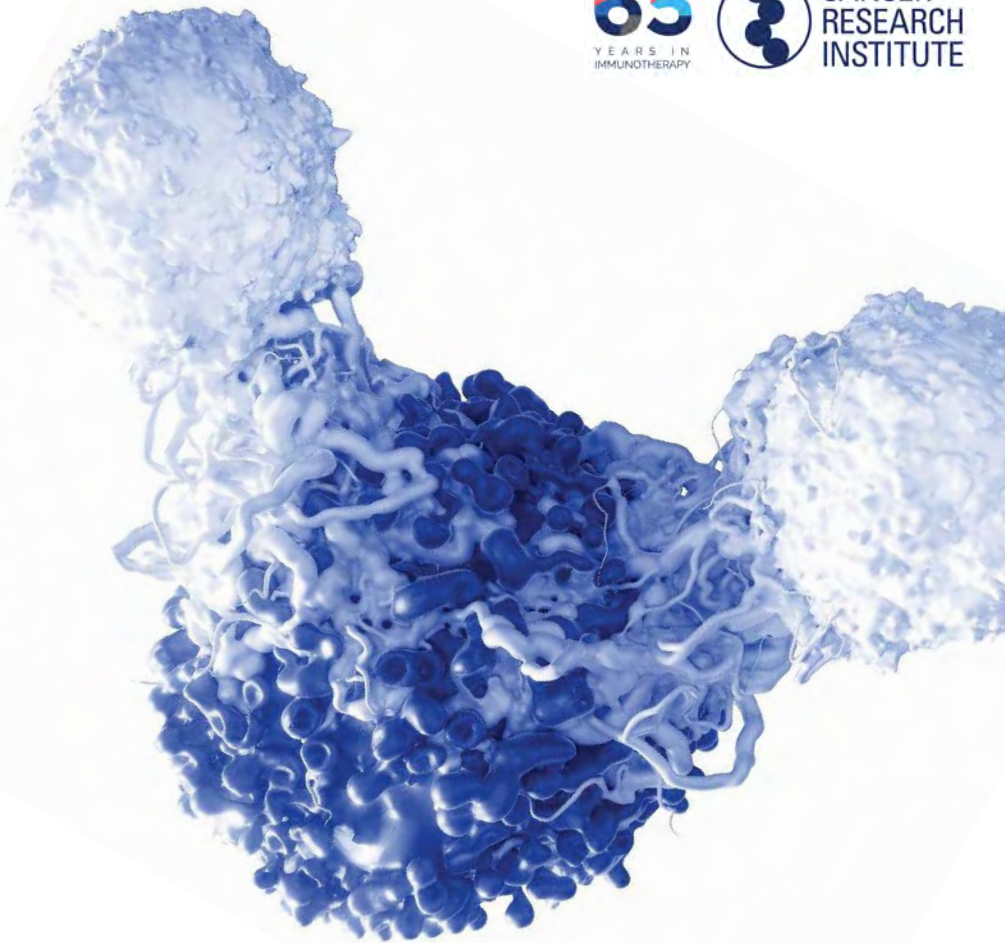
CANCER RESEARCH INSTITUTE

IMMUNOTHERAPY PATIENT SUMMIT

New York City September 15, 2018

65 YEARS IN IMMUNOTHERAPY

CANCER RESEARCH INSTITUTE



Brian Brewer

Cancer Research Institute

WELCOME

CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY
PATIENT SUMMIT

Our Host

Thank You to Columbia University Irving Medical Center

COLUMBIA UNIVERSITY
MEDICAL CENTER

Herbert Irving Comprehensive Cancer Center

CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY
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Our Sponsors

65 YEARS IN IMMUNOTHERAPY

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This event is made possible with generous support from:

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CANCER RESEARCH INSTITUTE IMMUNOTHERAPY PATIENT SUMMIT

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Our Educational Partners

Thank you to those who helped promote the summit

- Addario Lung Cancer Foundation
- But Doctor I Hate Pink (Ann Silberman)
- Cancer Support Community
- CancerCare
- Columbia University Irving Medical Center
- Fight Colorectal Cancer
- FORCE
- Gilda's Club Manhattan Clubhouse
- Imerman Angels
- Leukemia & Lymphoma Society
- Ludwig Cancer Research
- LUNGevity Foundation
- NewYork-Presbyterian/Columbia University Irving Medical Center
- Let Life Happen (Barbara Jacoby)
- Patient Empowerment Network
- Perlmutter Cancer Center at NYU Langone Health
- SHARE
- ThyCa Support Groups of New York
- Women to Women support group at Mount Sinai Medical Center
- Us TOO

Speakers

Scientific Experts

Charles G. Drake, M.D., Ph.D.
NewYork-Presbyterian/Columbia University Irving Medical Center

Catherine M. Diefenbach, M.D.
Perlmutter Cancer Center at NYU Langone Health

Gulam A. Manji, M.D., Ph.D.
NewYork-Presbyterian/Columbia University Irving Medical Center

Jedd D. Wolchok, M.D., Ph.D.
Memorial Sloan Kettering Cancer Center

Margaret Callahan, M.D., Ph.D.
Memorial Sloan Kettering Cancer Center

Patient Experts

Kerry Alvarado
Pancreatic cancer

Belur Bhagavan, M.D.
Bladder cancer

Gloria Garcia
Lung cancer

Karen Koehler
Chronic Lymphocytic Leukemia (CLL)

Adrienne Skinner
Ampullary cancer

Schedule of Events

65 YEARS IN IMMUNOTHERAPY

CANCER RESEARCH INSTITUTE

9:00 am	Registration and networking
10:00 am	Program commences **WELCOME** Brian Brewer **INTRO TO THE CANCER RESEARCH INSTITUTE** Jill O'Donnell Tormey, Ph.D.
10:15 am	**HEAR FROM THE EXPERTS** Immunotherapy Basics Charles G. Drake, M.D., Ph.D.
10:30 am	**RESEARCH UPDATES PANEL** Moderator Charles G. Drake, M.D., Ph.D. Panelists Catherine M. Diefenbach, M.D. Gulam A. Manji, M.D., Ph.D. Jedd D. Wolchok, M.D., Ph.D.
11:30 am	**PATIENT PERSPECTIVE** Karen Koehler
12:00 pm	Lunch and networking
1:00 pm	**LEARN ABOUT CLINICAL TRIALS**
1:15 pm	**IMMUNOTHERAPY PATIENT PANEL** Moderator Brian Brewer Panelists Kerry Alvarado Belur Bhagavan, M.D. Gloria Garcia Adrienne Skinner
2:00 pm	**BREAK**
2:15 pm	**BREAKOUT SESSIONS** Your choice of a deeper dive Q&A with our experts **General Immunotherapy** Charles G. Drake, M.D., Ph.D. **Melanoma** Margaret Callahan, M.D., Ph.D. **Blood Cancers** Catherine M. Diefenbach, M.D. **Gastrointestinal Cancers** Gulam A. Manji, M.D., Ph.D.
3:15 pm	Program closes
9:00 am – 4:00 pm	**CLINICAL TRIAL NAVIGATOR APPOINTMENTS** Appointments are available all day. If you didn't pre-register, but you are interested in scheduling an appointment, please visit the Clinical Trial Navigator desk for more information.

Directory of Events

Ground Floor

Lobby
- Registration
- Check-in for Clinical Trial Navigator appointments
- Lunch,* 12:00 pm

Floors 2 & 3

Auditorium
- General Session, 10:00 am
- Breakout Session I: General Immunotherapy, 2:15 pm

Floor 4

Room 401
- Lunch,* 12:00 pm

Rooms 404/405
- Additional Lunch Seating,* 12:00 pm

Floor 9

Room 902/903
- Breakout Session II: Blood Cancers, 2:15 pm

Floor 12

Rooms 1201A & 1201B
- Clinical Trial Navigator appointments

Rooms 1202/1203
- Breakout Session III: Melanoma, 2:15 pm

Floor 14

Rooms 1402/1403
- Breakout Session IV: Gastrointestinal Cancers, 2:15 pm

*Lunch will be served in room 401 with additional seating in rooms 404/405. A second lunch buffet will be set up in the lobby on the ground floor.

Thank You!

You will receive two emails after the summit:

1. **A survey** to share your feedback on the summit as well as insights into future programming.

2. **Information** from the summit day, including this presentation and instructions on how to use our Clinical Trial Finder service.

65 YEARS IN IMMUNOTHERAPY

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Jill O'Donnell-Tormey, Ph.D.

Cancer Research Institute

WELCOME

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IMMUNOTHERAPY **PATIENT** SUMMIT

Basics of Immunotherapy

65 YEARS IN IMMUNOTHERAPY

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Charles G. Drake M.D. / Ph.D.

Director GU Medical Oncology
Co-Director: Immunotherapy Program
Associate Director for Clinical Research
Professor of Oncology and Urology
Herbert Irving Cancer Center at Columbia University

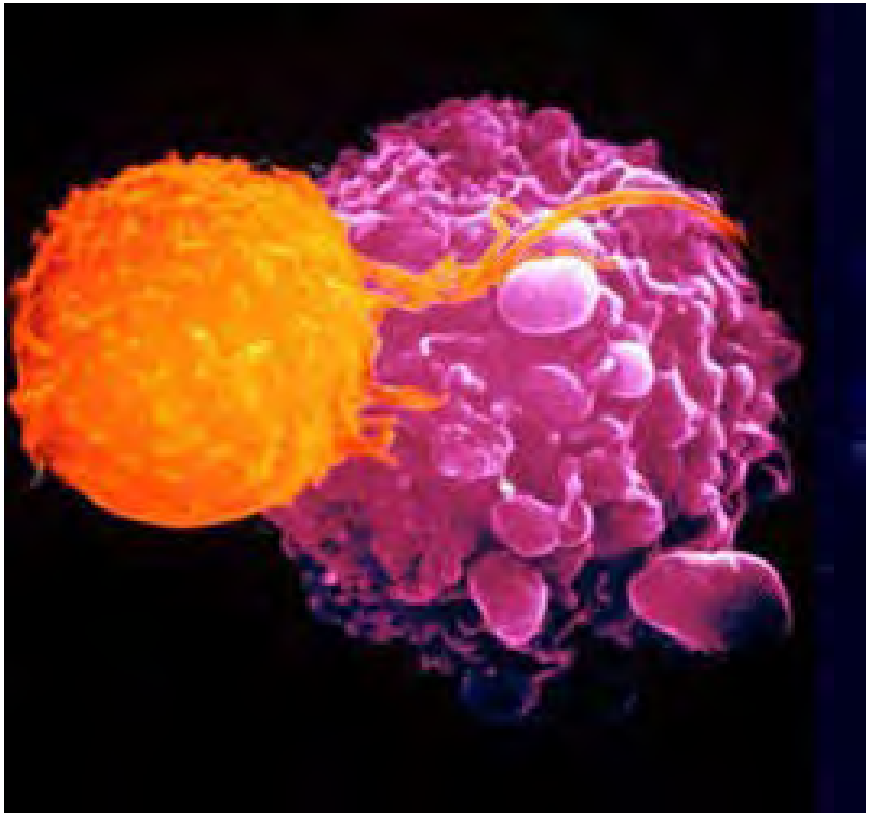
NewYork-Presbyterian

Columbia University Medical Center
Herbert Irving Comprehensive Cancer Center

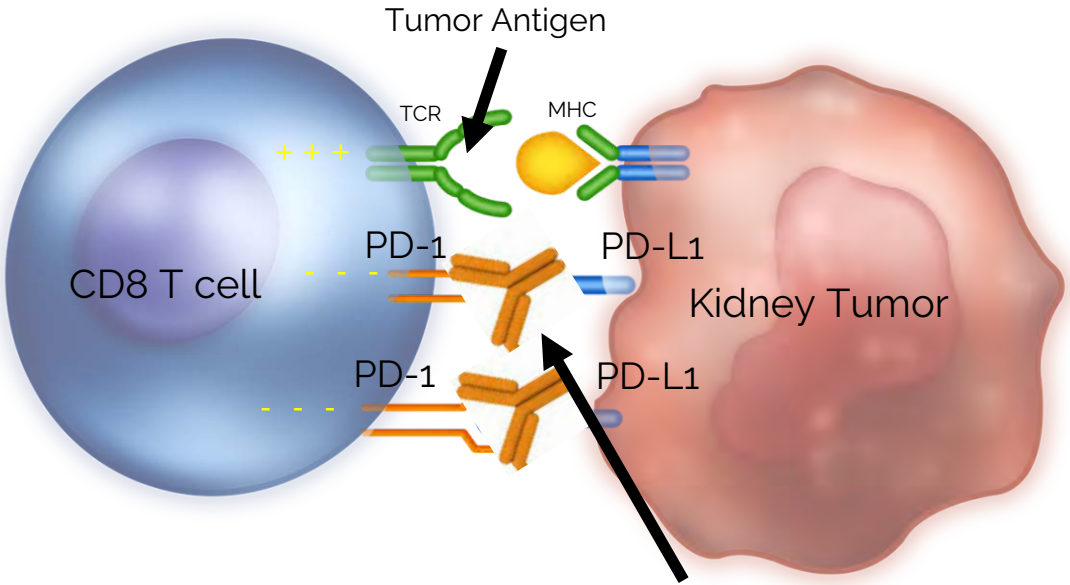
Outline

- T Cells
- Activating T Cells in Tumors
- Activating T Cells Outside of Tumors
- Combination Immunotherapy
- Biomarkers and Biopsies

CD8 T Cells Are Born to Kill

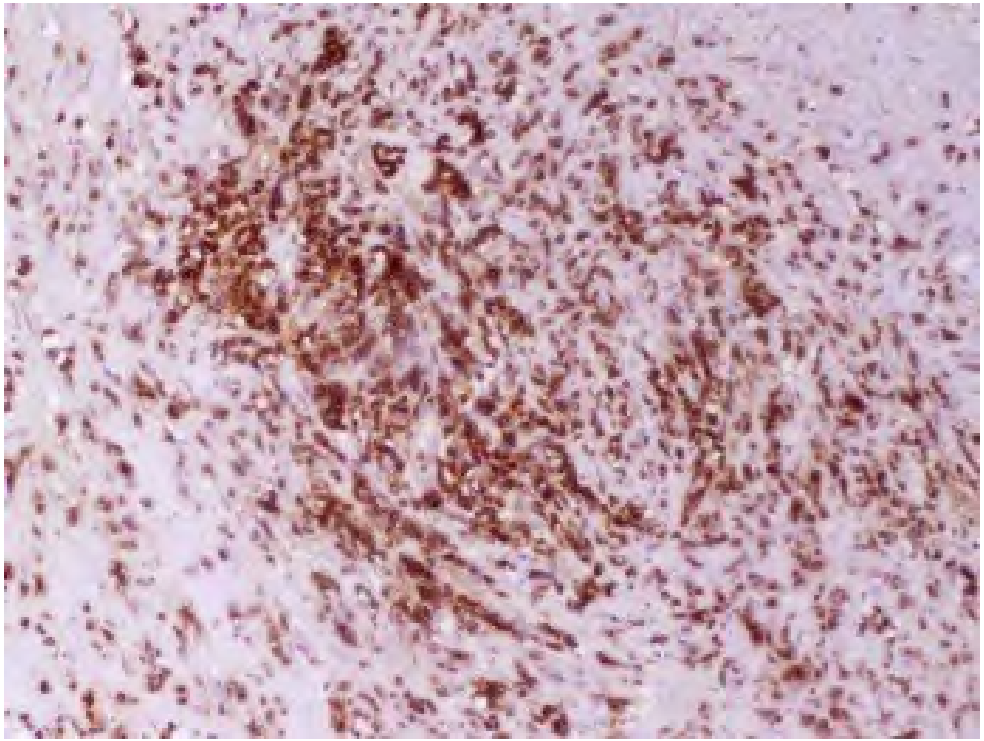


Why are Those Killer T Cells Not Killing?



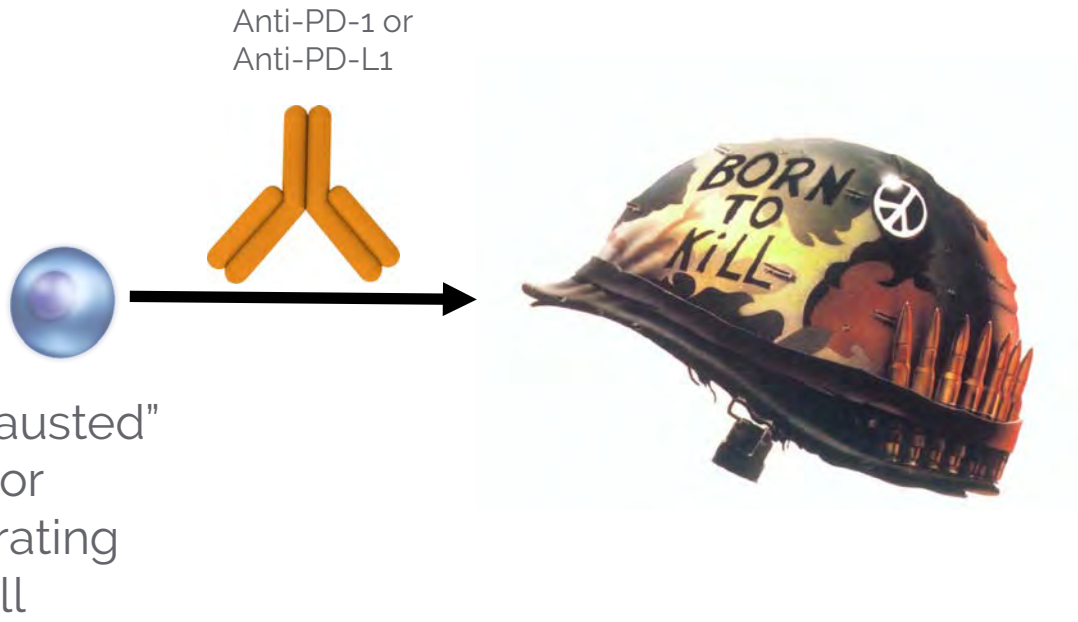
CD8 T Cells Are Being Held in Check (Exhausted)
WHEN PD-L1 Is Expressed

Killer T Cells in Tumors



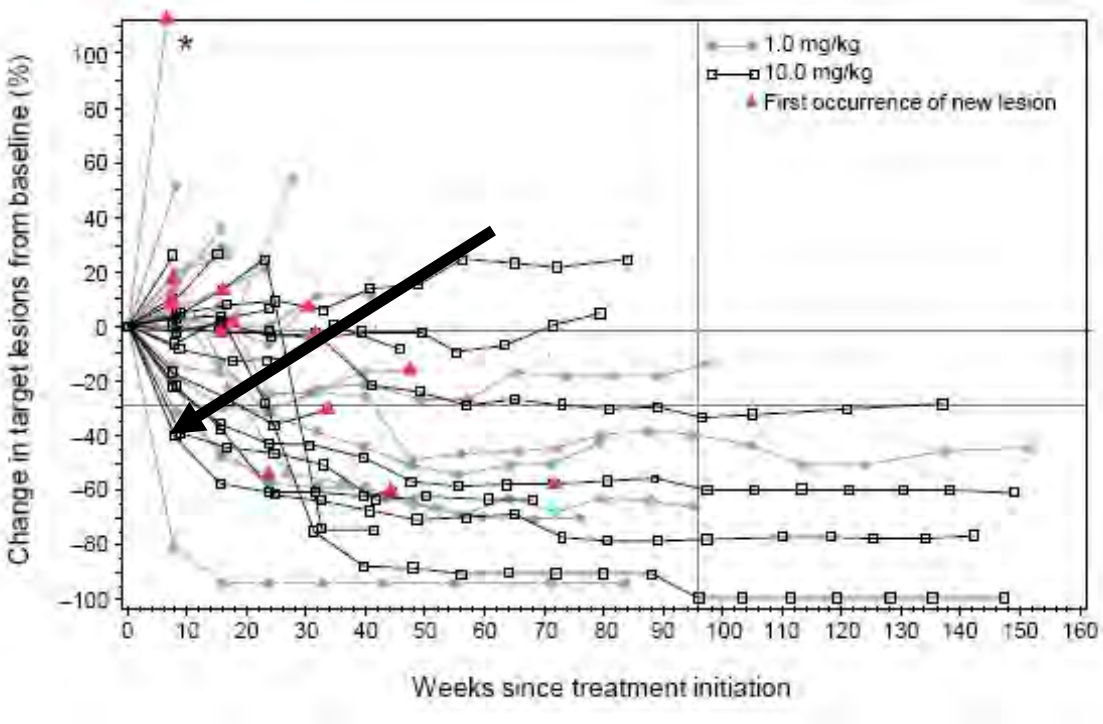
Brown Staining = CD8 T Cells

Blocking PD-1 (or PD-L1) Allows T Cells to Regain the Capacity to Kill



Rapid Tumor Shrinkage (In Some Patients) Evidence of Killing

Lower is Better



Drake CG et al Journal of Clinical Oncology, 2013 ASCO Annual Meeting Abstracts. Vol 31, No 15_suppl (May 20 Supplement), 2013: 4514 ASCO 2013

Not Just a Line on a Graph . . . .

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2002: Surgery to remove kidney cancer

2004: Relapse with multiple lung tumors
Treated on sequential clinical trials

2008: Multiple metastatic cancer lesions in lungs, bone, soft tissue

2008: Enrolled in Phase I Trial of Experimental Immune Drug

2010: Complete Response

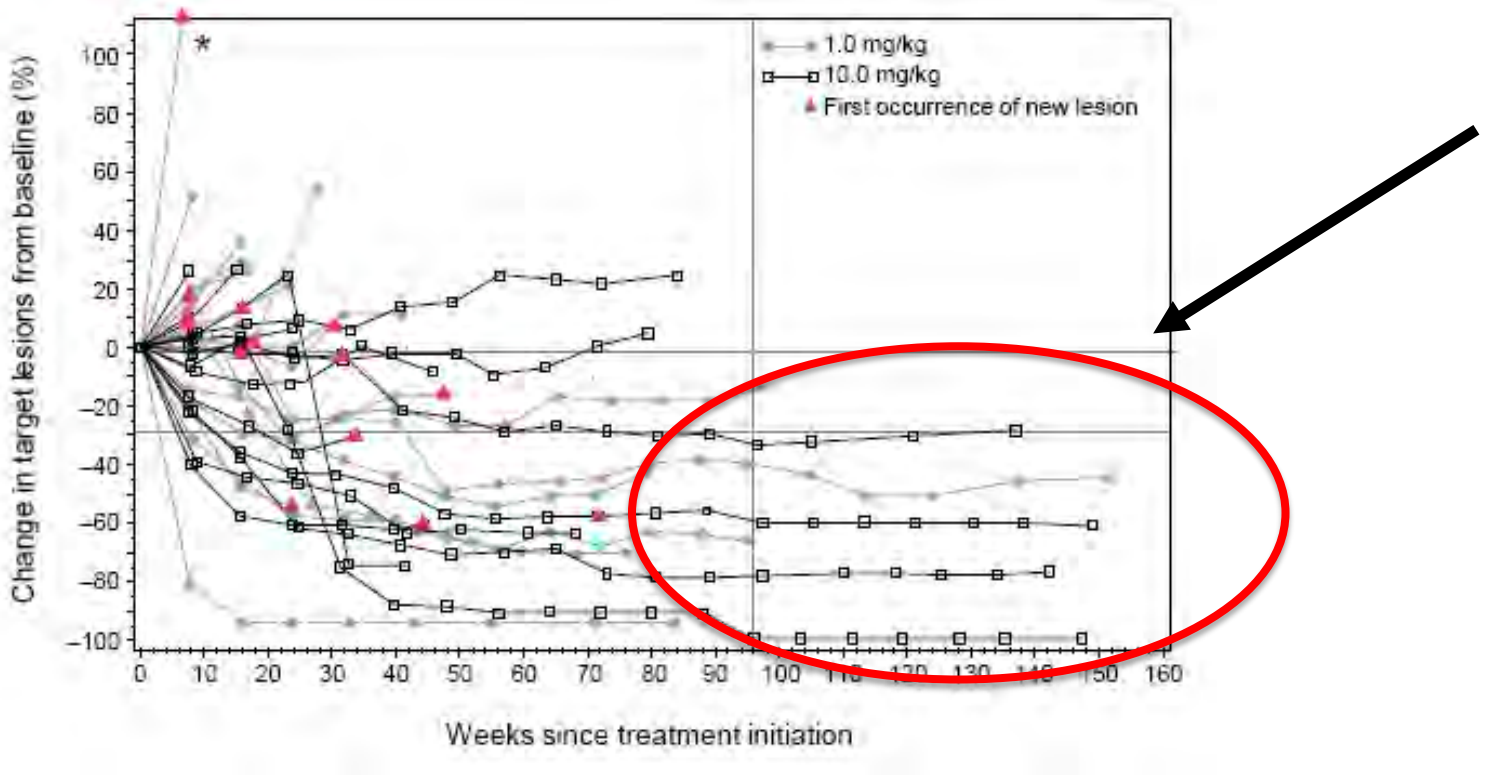
- Patient received 3 study treatments
- Limited side effects
- Rapid treatment response
- Cancer-free for 9+ years

January
First treatment

March
2 month evaluation

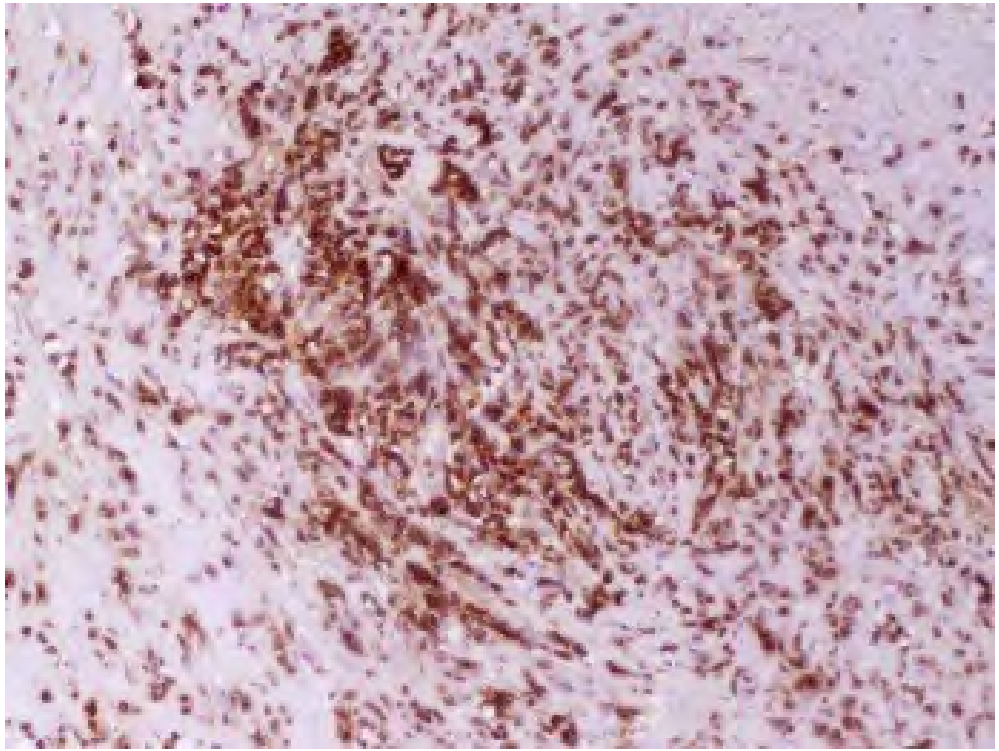
Long Term Responses Off Treatment

Evidence for T Cell Memory ?



Drake CG et al Journal of Clinical Oncology, 2013 ASCO Annual Meeting Abstracts.
Vol 31, No 15_suppl (May 20 Supplement), 2013: 4514 ASCO 2013

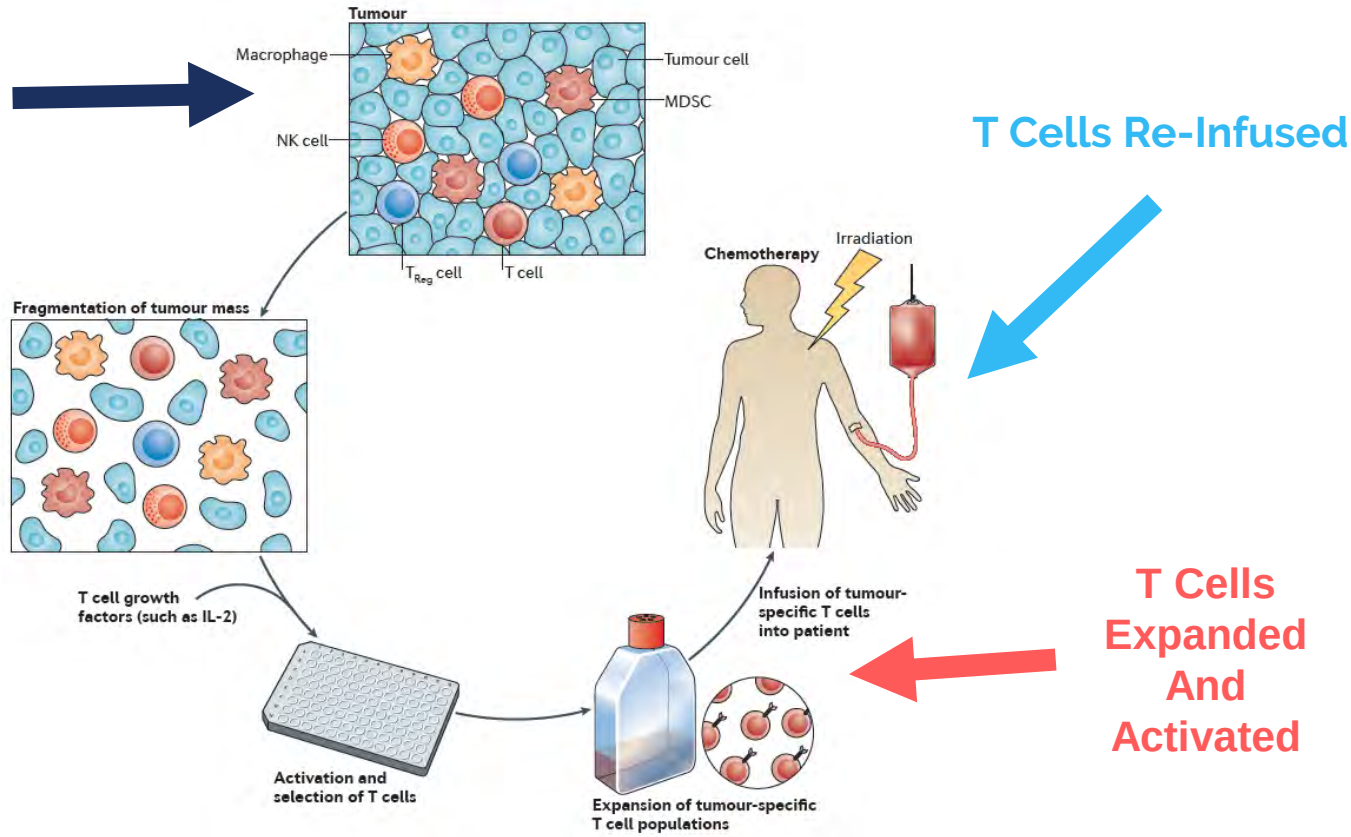
Other Approaches



Brown Staining = CD8 T Cells

MORE Is Better: Adoptive T Cell Transfer

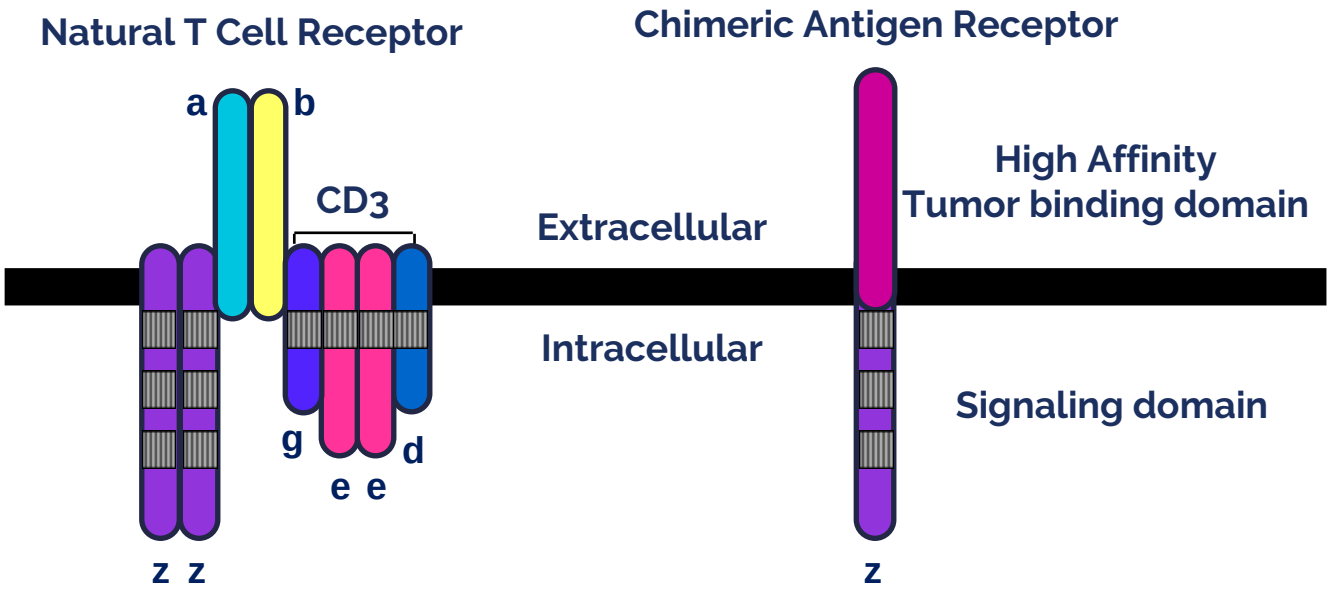
T cells isolated from patient



T Cells Re-Infused

T Cells Expanded And Activated

BETTER Is Better: Chimeric Antigen Receptor T Cells (CAR-T)



Courtesy of. Carl June, U Penn

SEARCH

The New York Times

HEALTH

In Girl's Last Hope, Altered Immune Cells Beat Leukemia

By DENISE GRADY DEC. 9, 2012

Emma Whitehead, with her mother, Kari. Last spring, Emma was near death from acute lymphoblastic leukemia but is now in remission after an experimental treatment at the Children's Hospital of Philadelphia.
Jeff Swensen for The New York Times

This Means CAR-T Cells

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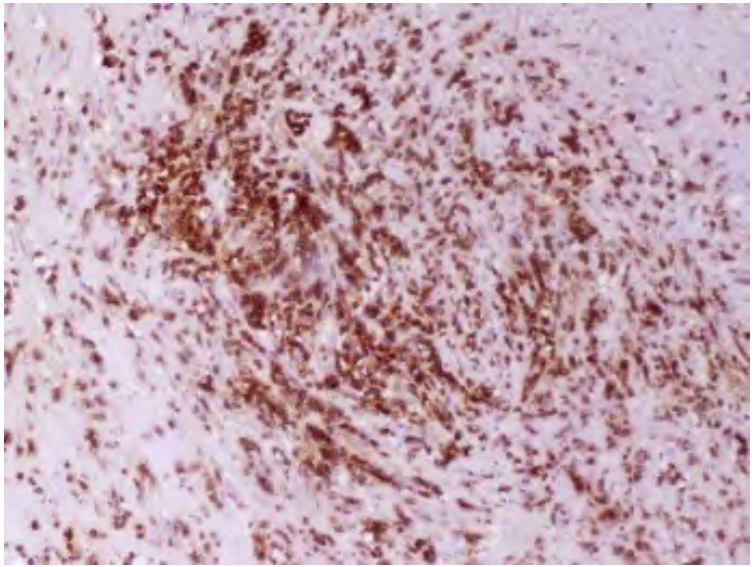
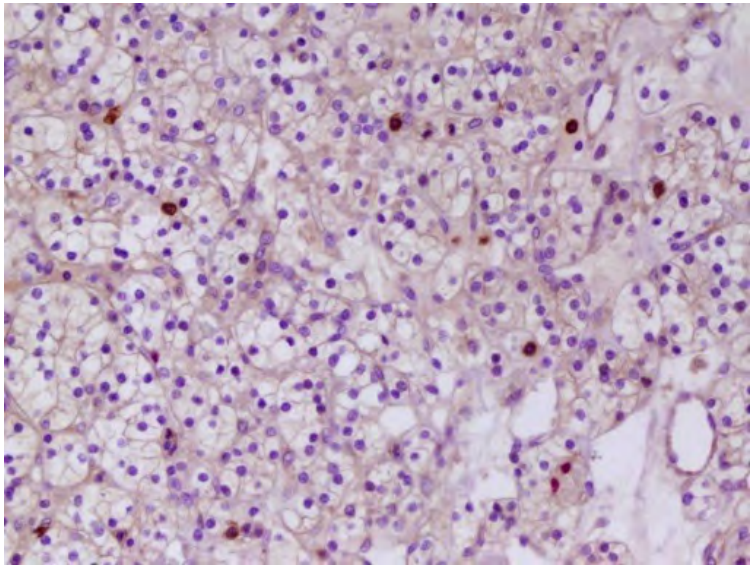
Combination Approaches (Making a Cold Tumor Hot)



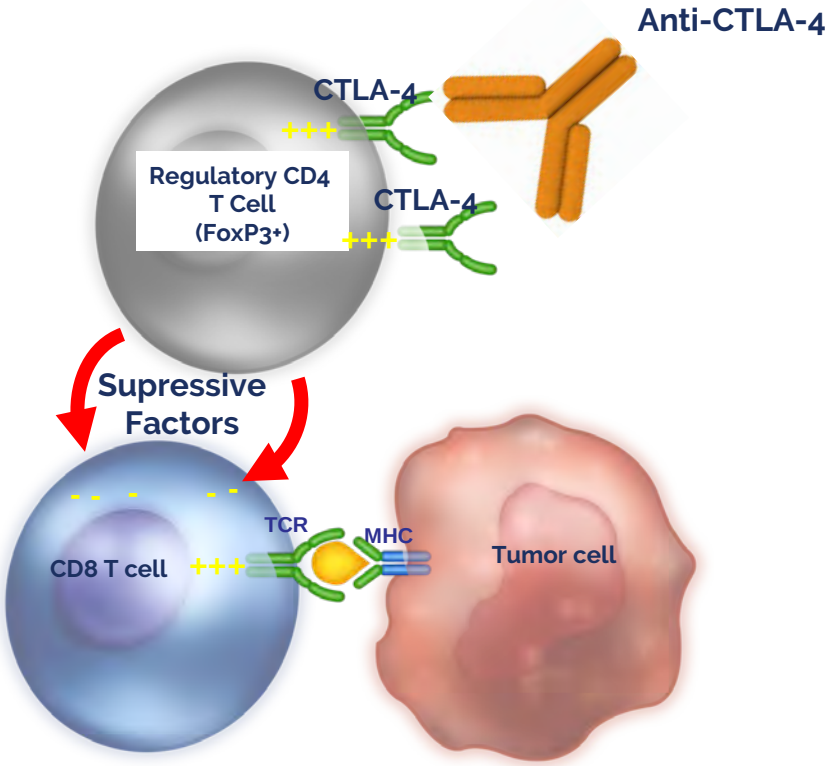
Kidney Tumor with T Cells



Kidney Tumor

Brown Staining = CD8

The Tumor Microenvironment Is a VERY Unfriendly Place



Side Effects of Immunotherapy

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Table 2. Highest Grade of Selected Treatment-Related Adverse Events That Occurred in at Least One of the Patients Who Received the Concurrent Regimen.*

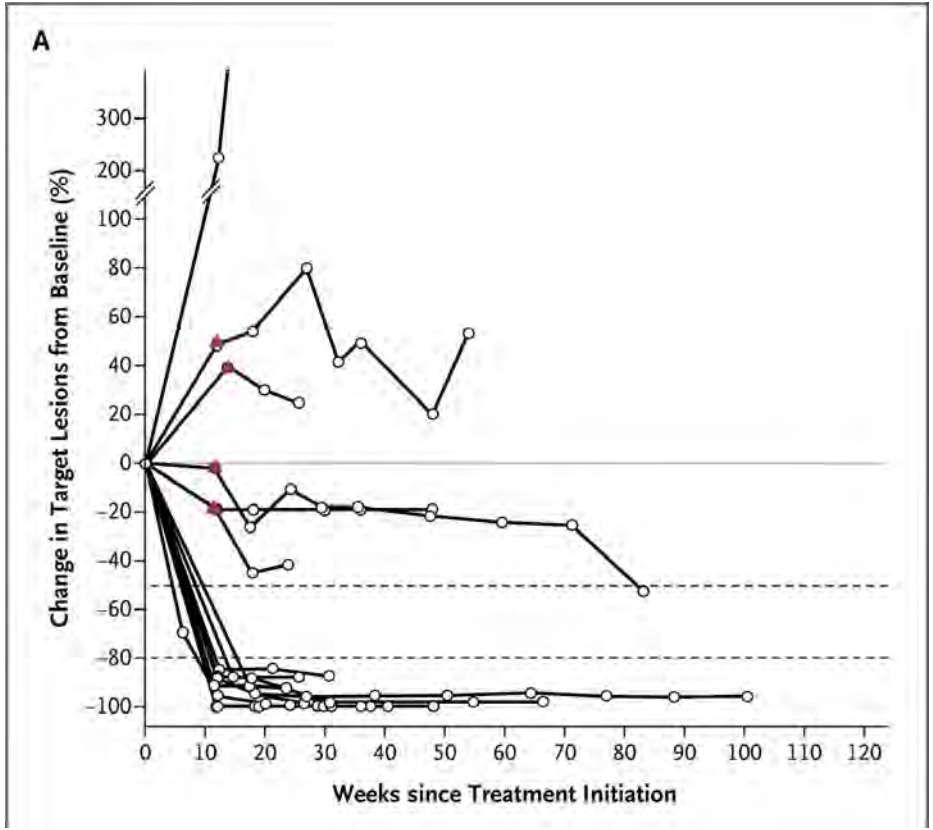
Event	Cohort 1 (N=14)		Cohort 2 (N=17)		Cohort 2a (N=16)		Cohort 3 (N=6)		All Patients in Concurrent-Regimen Group (N=53)	
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
	number of patients (percent)									
Pneumonitis	1 (7)	0	2 (12)	1 (6)	0	0	0	0	3 (6)	1 (2)
Endocrinopathy	1 (7)	0	3 (18)	0	1 (6)	0	2 (33)	1 (17)	7 (13)	1 (2)
Hypothyroidism	0	0	2 (12)	0	0	0	0	0	2 (4)	0
Hypophysitis	0	0	1 (6)	0	0	0	1 (17)	1 (17)	2 (4)	1 (2)
Thyroiditis	0	0	1 (6)	0	1 (6)	0	1 (17)	0	3 (6)	0
Adrenal insufficiency	0	0	2 (12)	0	0	0	0	0	2 (4)	0
Hyperthyroidism	0	0	1 (6)	0	0	0	1 (17)†		2 (4)†	0
Thyroid-function results abnormal	1 (7)	0	0	0	0	0	0	0	1 (2)	0
Hepatic disorder	4 (29)	3 (21)	5 (29)	3 (18)	2 (12)	1 (6)	1 (17)	1 (17)	12 (23)	8 (15)
Aspartate aminotransferase increased	4 (29)	3 (21)	4 (24)	2 (12)	2 (12)	1 (6)	1 (17)	1 (17)	11 (21)	7 (13)
Alanine aminotransferase increased	3 (21)	2 (14)	5 (29)	3 (18)	2 (12)	0	1 (17)	1 (17)	11 (21)	6 (11)
Gastrointestinal disorder	5 (36)	1 (7)	6 (35)	2 (12)	6 (38)	2 (13)	3 (50)	0	20 (38)	5 (9)
Diarrhea	5 (36)	0	5 (29)	1 (6)	5 (31)	2 (13)	3 (50)	0	18 (34)	3 (6)
Colitis	1 (7)	1 (7)	2 (12)	1 (6)	1 (6)	0	1 (17)	0	5 (9)	2 (4)
Renal disorder	1 (7)	1 (7)	1 (6)	1 (6)	1 (6)	1 (6)	0	0	3 (6)	3 (6)
Blood creatinine increased	1 (7)	1 (7)	1 (6)	1 (6)	1 (6)	1 (6)	0	0	3 (6)	3 (6)
Acute renal failure	0	0	1 (6)	1 (6)	1 (6)	1 (6)	0	0	2 (4)	2 (4)
Renal failure	0	0	1 (6)	1 (6)	0	0	0	0	1 (2)	1 (2)
Tubulointerstitial nephritis	1 (7)	0	0	0	0	0	0	0	1 (2)	0
Skin disorder	10 (71)	1 (7)	14 (82)	0	10 (62)	1 (6)	3 (50)	0	37 (70)	2 (4)
Rash	8 (57)	1 (7)	11 (65)	0	7 (44)	1 (6)	3 (50)	0	29 (55)	2 (4)
Pruritus	6 (43)	0	11 (65)	0	7 (44)	0	1 (17)	0	25 (47)	0
Urticaria	0	0	0	0	1 (6)	0	0	0	1 (2)	0
Blister	0	0	1 (6)	0	0	0	0	0	1 (2)	0
Infusion-related reaction	0	0	1 (6)	0	0	0	0	0	1 (2)	0

* Only the highest grade of event was counted for each patient. Adverse events that require more frequent monitoring or intervention with immune suppression or hormone replacement are listed, according to a prespecified list of terms from the *Medical Dictionary for Regulatory Activities*, version 15.1. The dose levels in the cohorts were as follows: cohort 1 received 0.3 mg of nivolumab per kilogram of body weight and 3 mg of ipilimumab per kilogram, cohort 2 received 1 mg of nivolumab per kilogram and 3 mg of ipilimumab per kilogram, cohort 2a received 3 mg of nivolumab per kilogram and 1 mg of ipilimumab per kilogram, and cohort 3 received 3 mg of nivolumab per kilogram and 3 mg of ipilimumab per kilogram. The doses in cohort 3 exceeded the maximum doses that were associated with an acceptable level of adverse events, and the doses in cohort 2 were identified as the maximum doses that were associated with an acceptable level of adverse events. The numbers reported for the specific adverse events within an organ category may be greater than the total number reported for the organ category because patients who had more than one adverse event were counted for each event but were counted only once for the organ category.

† Data include one patient with an event of unknown grade.

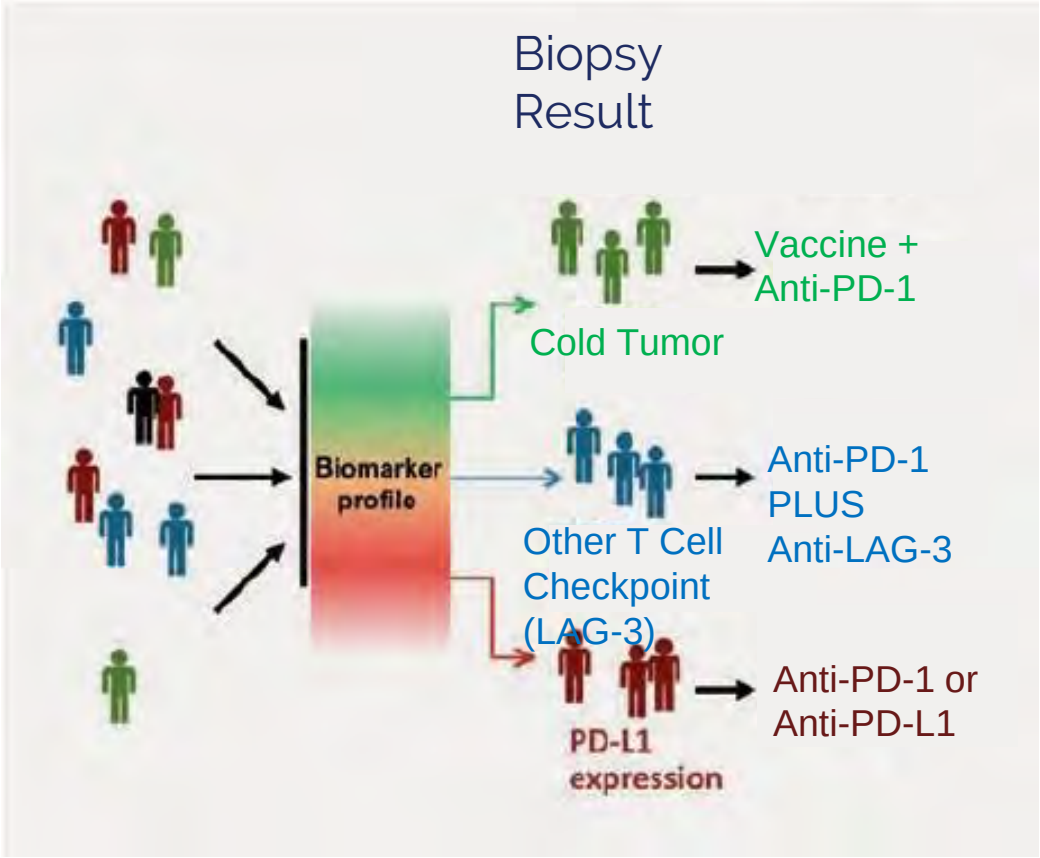
The NEW ENGLAND JOURNAL of MEDICINE

Immunotherapy Treatment Results

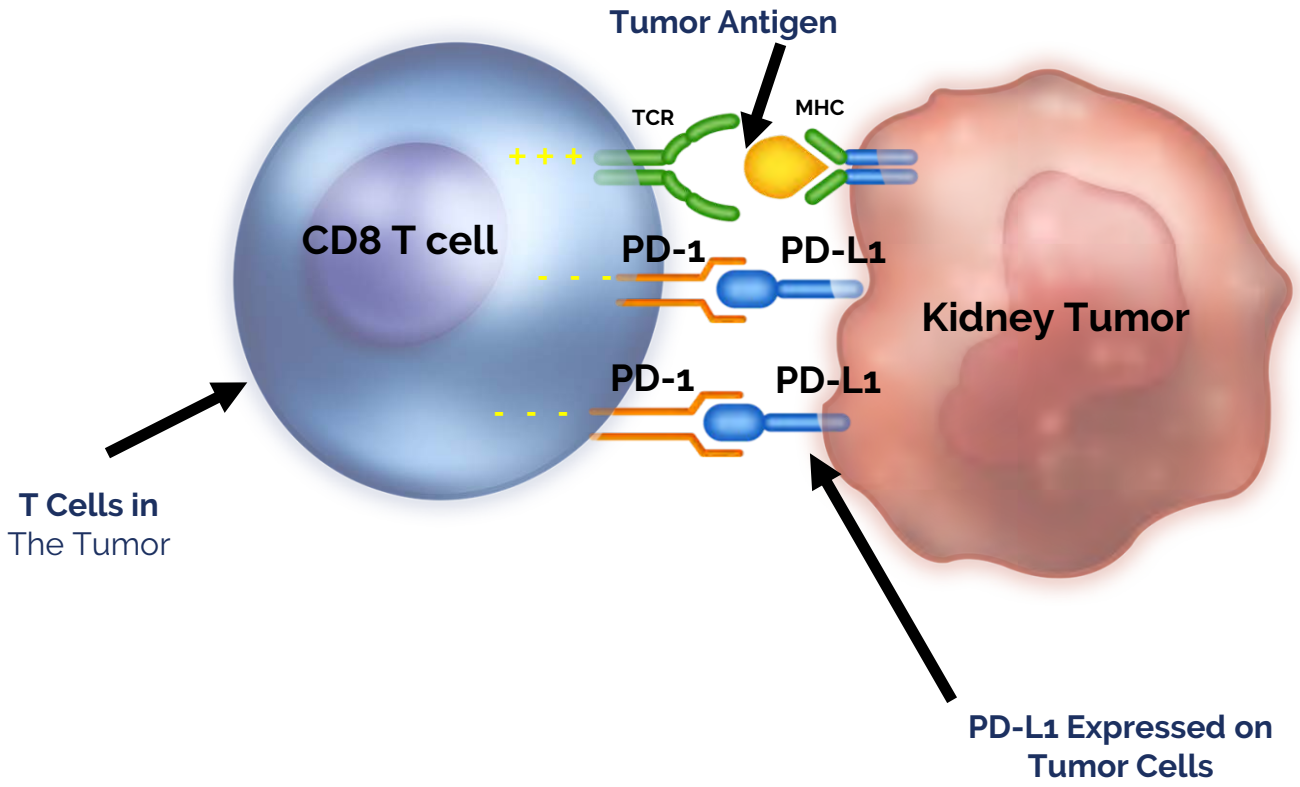


The NEW ENGLAND JOURNAL of MEDICINE

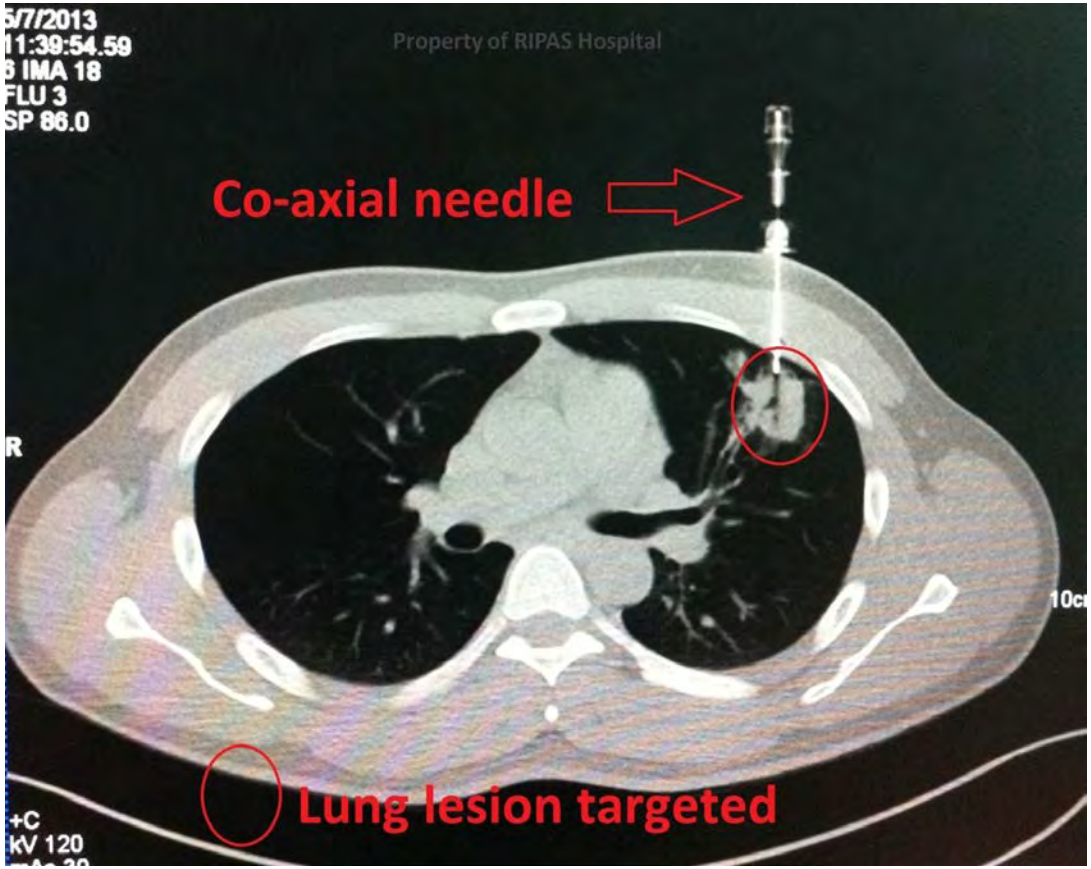
Choosing the Right Drug for the Right Patient: Biomarkers



PD-L1 Is a Fairly Good Biomarker

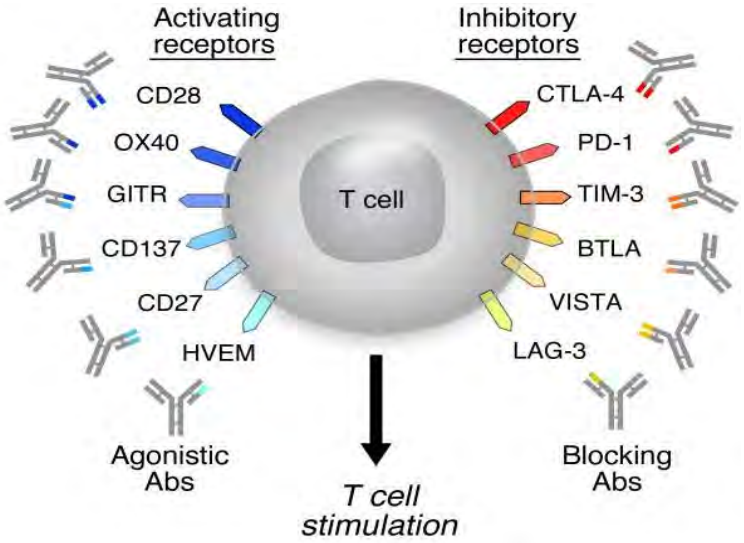


How to Find New / Better Biomarkers ?



The Future:

Targets on T Cells



Targets in the Tumor Microenvironment

- IDO
- Adenosine / A2A Receptor
- TGF-Beta
- Interleukin 8
- CSF-1
- NLRP3

Nature. 2011 480:480-9

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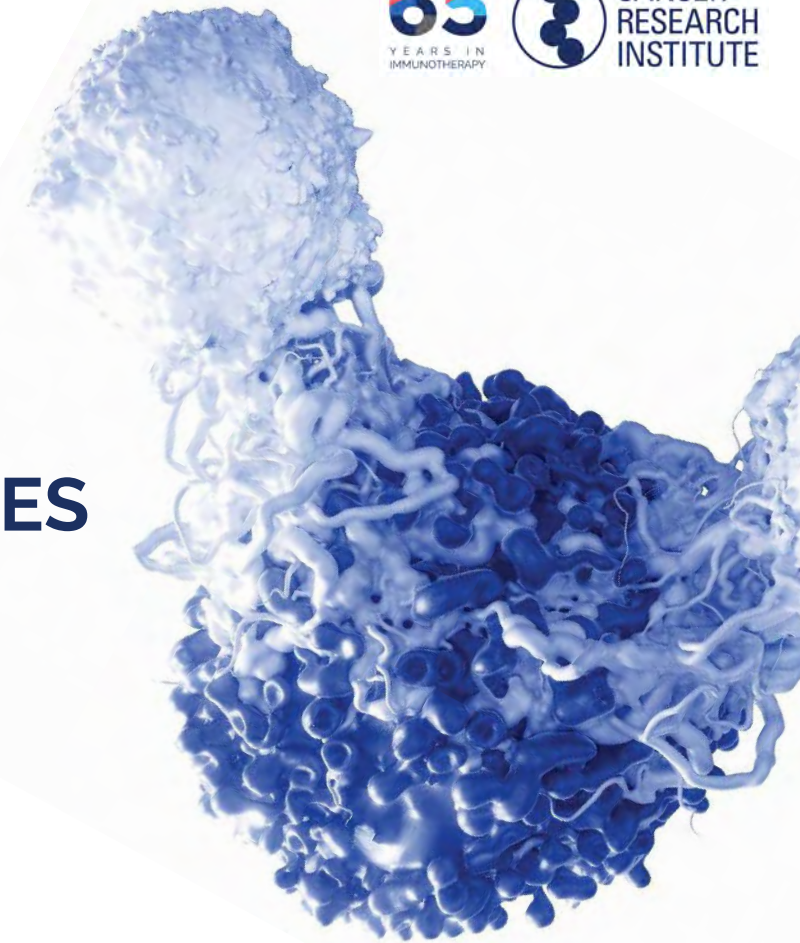

Panel Discussion

LATEST RESEARCH UPDATES

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Scientific Panel

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Moderator

Charles G. Drake, M.D., Ph.D.

Panel

Catherine M. Diefenbach, M.D.
Blood cancers

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Melanoma

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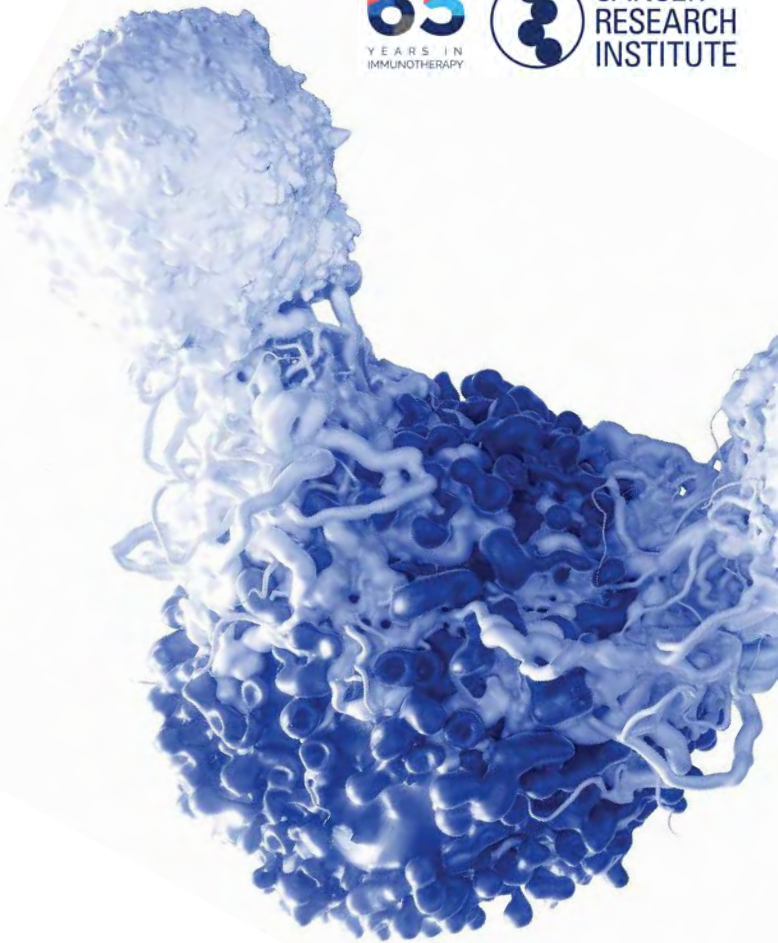

Karen Koehler

Surviving Chronic Lymphocytic Leukemia (CLL)

PATIENT PERSPECTIVE

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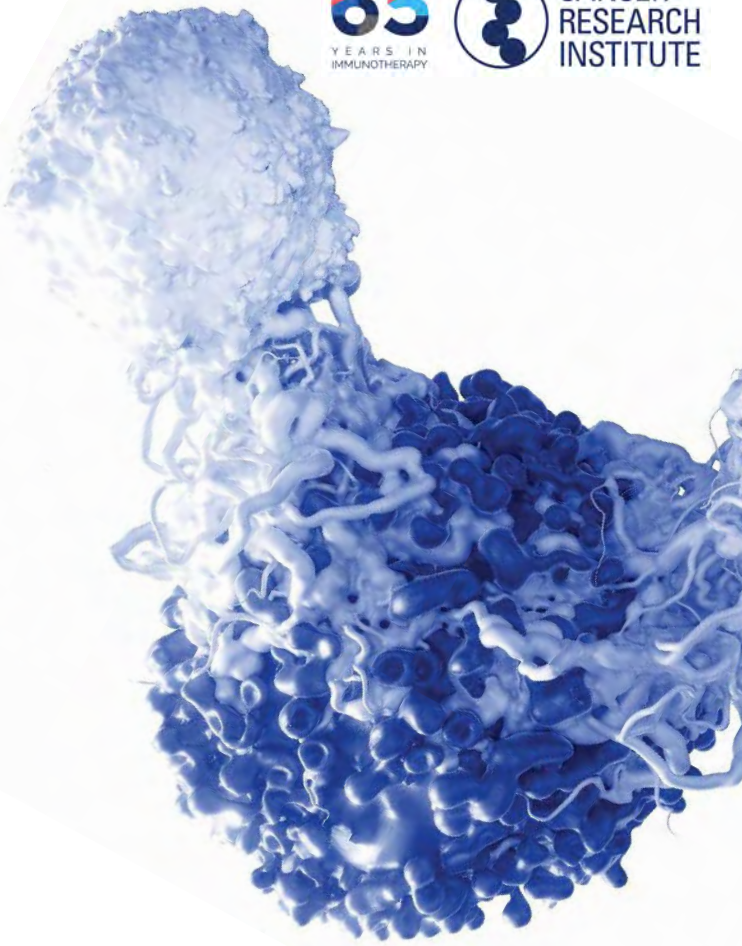
Lunch and Networking

Floor 4: Room 401

Additional seating in rooms 405/405 and ground floor lobby



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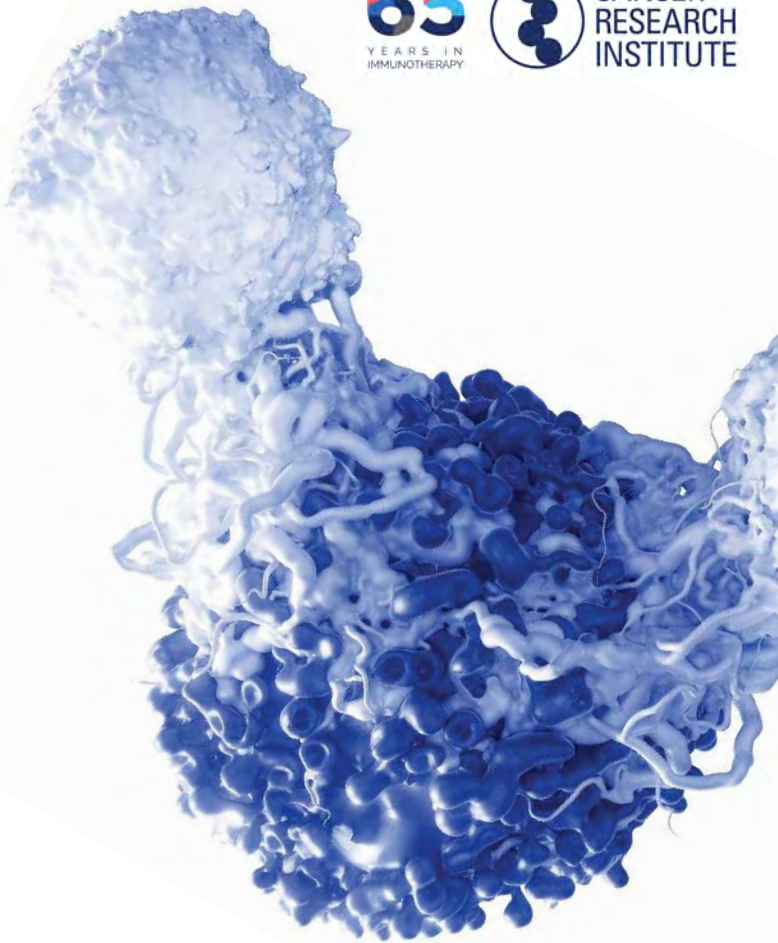

Brian Brewer

Cancer Research Institute

LEARN ABOUT CLINICAL TRIALS

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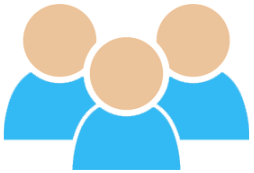
What Are Clinical Trials?



- Research studies that involve people
- Designed to answer specific questions about new and existing treatments
- Aim to improve treatments and the quality of life for people with disease

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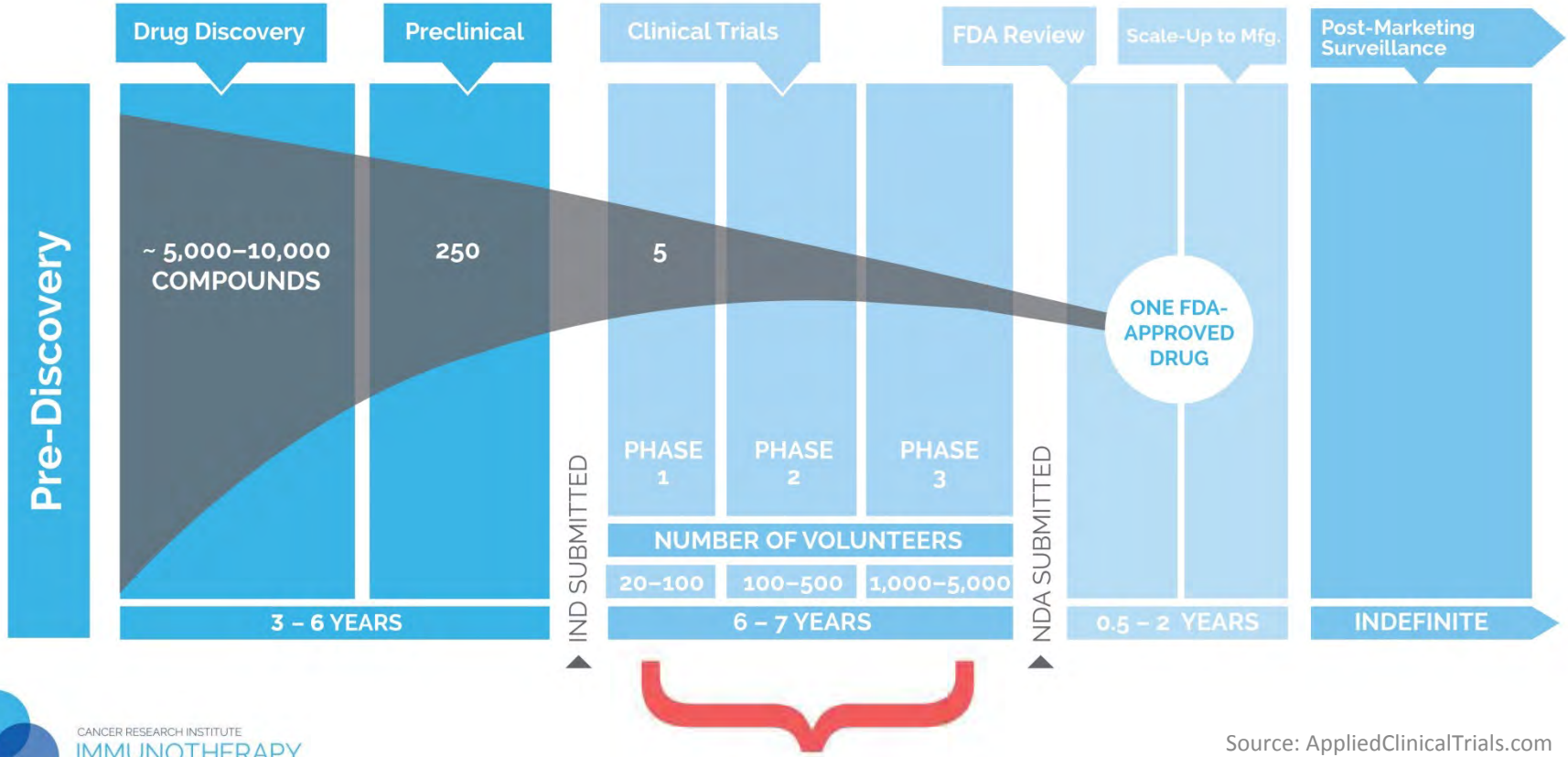
Getting from Discovery to Approval



Source: AppliedClinicalTrials.com

What Are Clinical Trial Phases?

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Phase 1

Is the treatment safe?

Purpose:

- First study in humans
- Find best dose, delivery method, and schedule
- Monitor for side effects
- Determine safety

Number of people: 20-100

Phase 2

Does it work?

Purpose:

- Look for effect on specific type(s) of cancer
- Continue monitoring for side effects and safety

Number of people: 100-500

Phase 3

Does it work better?

Purpose:

- Compare new treatment (or new use of a treatment) with current standard treatment
- Determine risk vs. benefit

Number of people: 1,000-5k+

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Pros and Cons of Clinical Trials

Potential Advantages	Potential Disadvantages
Access to best possible care	Unknown side effects or risks
Receiving new drugs before they're widely available	Unknown benefits—drugs may not work as intended
Close monitoring by medical team	Not all patients may benefit
Chance to play active role in healthcare and research	Frequent tests and clinic visits
Help future generations	Possible need to travel to trial sites

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Questions to Ask Before Volunteering

- Why is this trial being done?
- Why is it believed that the treatment being studied may be better than the standard treatment?
- What are my other options (standard treatments, other trials)?
- How did patients do in any previous studies of this treatment?
- How will the doctor know if treatment is working?
- How long will the trial last?

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Questions to Ask Before Volunteering

- Can I continue to receive this treatment after the trial ends?
- What kinds of procedures or tests are involved?
- What impact with the trial have on my daily life?
- Will I have to travel for treatment? Will I be compensated?
- How often will I need to travel to receive treatment?
- Will I be hospitalized as part of the trial?
- What costs (if any) will be my responsibility to pay?

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Getting into a Clinical Trial Isn't Always a Given

Trials are designed to ask specific questions, and must adhere strictly to entry criteria to ensure data is accurate and meaningful.

This also helps ensure patients who could be made worse by treatment are not exposed to the risk.

Common criteria include:

- **cancer type or stage**
- **treatment history**
- **genetic factors**
- **age**
- **medical history**
- **current health status**

Clinical Trials: Myth versus Fact

I might only get placebo
("sugar pill") instead of treatment.

Placebos are rarely used and never given
in the absence of some form of treatment.

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Clinical Trials: Myth versus Fact

Trials are only for people who have run out of treatment options (a “last resort”).

Clinical trials are designed for people with cancer of all types and stages.

Patient Resource, “Understanding Clinical Trials: A Guide for Patients and Their Families”

Clinical Trials: Myth versus Fact

I need to travel to a large hospital or cancer center to participate in a clinical trial.

Trials take place at local hospitals, cancer centers, and doctors' offices in all parts of the country, in both urban and rural areas.

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Clinical Trials: Myth versus Fact

My health insurance doesn't cover the cost of care in a clinical trial.

Doctor visits, hospital stays, and certain testing procedures may be covered by insurance. Research costs are typically covered by the trial sponsor.

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Clinical Trials: Myth versus Fact

Signing a consent form “locks” me into staying in a trial.

Fact: You are free to change your mind for any reason about participating in a trial anytime before or during a trial.

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Clinical Trials: Myth versus Fact

I will be made to feel like a "guinea pig" experiment.

Fact: The overwhelming majority of trial participants say they were treated with dignity and respect, and report having had a positive experience in a trial.

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Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

Clinical Trials: Myth versus Fact

Clinical trials aren't safe.

Fact: Safeguards including an Institutional Review Board, Data and Safety Monitoring Board, and an ongoing informed consent process ensure patients' rights and safety are protected.

Patient Resource, "Understanding Clinical Trials: A Guide for Patients and Their Families"

A Word About Informed Consent

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Informed consent = having all the facts before and during a trial

- Study purpose
- Length of time of the study
- Predictable risks
- Possible benefits
- Expectations
- Patient's rights

- Treatment alternatives
- Patient health monitoring
- Safeguards in place
- How to withdraw from study

Be bold in asking for details.
It's YOUR treatment plan.

How Can I Find a Clinical Trial?

- Ask your doctor
- Ask another doctor if necessary…
- Contact a patient advocacy organization
  - Seek assistance from a clinical trial navigator, if offered
  - CRI Clinical Trial Finder: 1 (855) 216-0127
- Search online
  - https://www.cancerresearch.org/patients/clinical-trials
  - https://clinicaltrials.gov/

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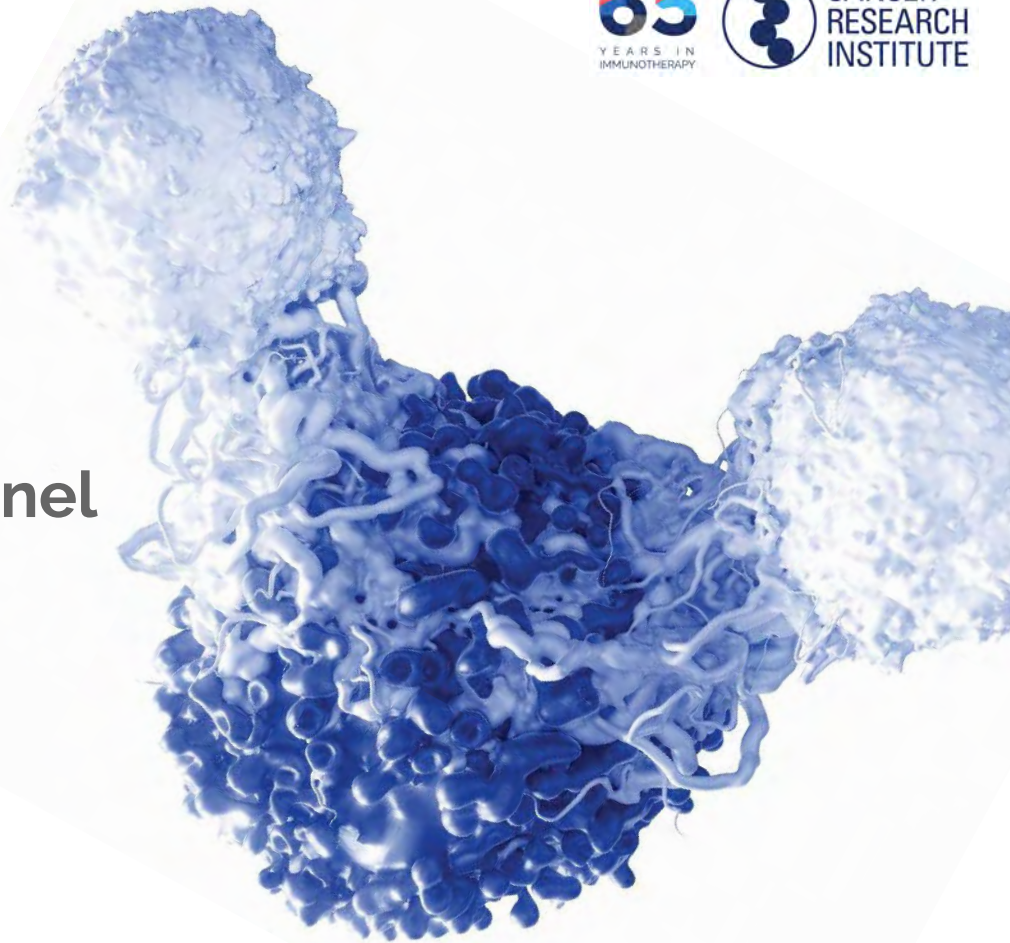

Panel Discussion

Immunotherapy Patient Panel

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Patient Panel

Moderator	Panel
Brian Brewer	**Kerry Alvarado** Pancreatic cancer **Belur Bhagavan, M.D.** Bladder cancer **Gloria Garcia** Lung cancer **Adrienne Skinner** Ampullary cancer

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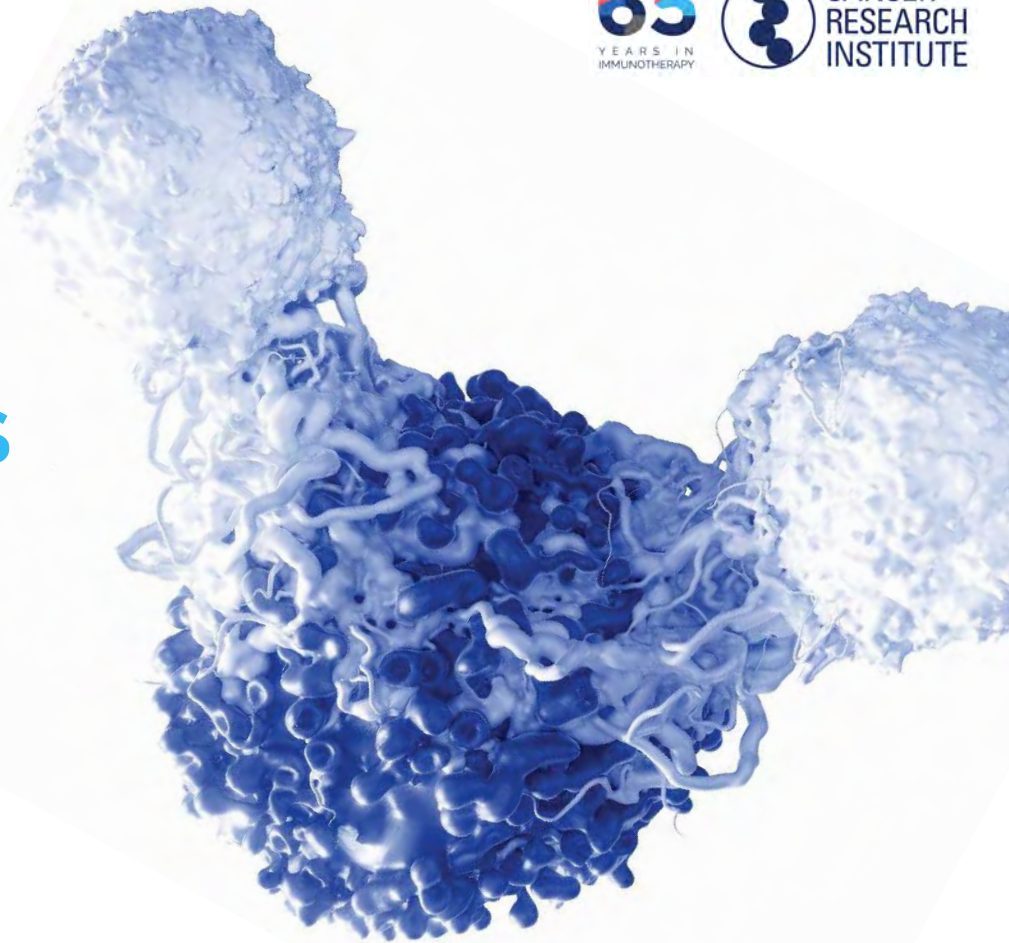
BREAKOUT SESSIONS



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Breakout Session Rooms

General Immunotherapy Charles G. Drake, M.D., Ph.D.	Auditorium Floors 2 & 3
Blood cancers Catherine M. Diefenbach, M.D.	Rooms 902/903 Floor 9
Melanoma Margaret Callahan, M.D., Ph.D.	Rooms 1202/1203 Floor 12
Gastrointestinal cancers Gulam A. Manji, M.D., Ph.D.	Room 1402/1403 Floor 14

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Thank you to those who helped promote the summit

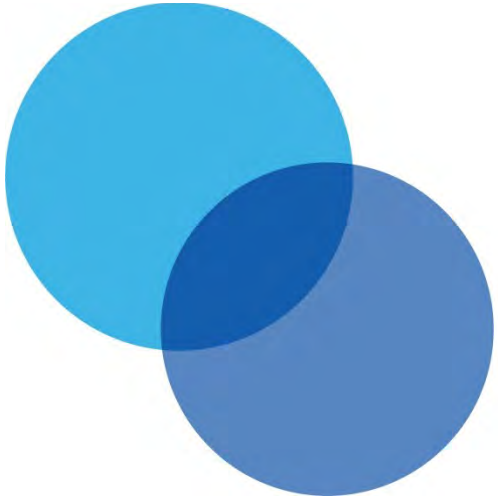
- Addario Lung Cancer Foundation
- But Doctor I Hate Pink (Ann Silberman)
- Cancer Support Community
- CancerCare
- Columbia University Irving Medical Center
- Fight Colorectal Cancer
- FORCE
- Gilda's Club Manhattan Clubhouse
- Imerman Angels
- Leukemia & Lymphoma Society
- Ludwig Cancer Research
- LUNGevity Foundation
- NewYork-Presbyterian/Columbia University Irving Medical Center
- Let Life Happen (Barbara Jacoby)
- Patient Empowerment Network
- Perlmutter Cancer Center at NYU Langone Health
- SHARE
- ThyCa Support Groups of New York
- Women to Women support group at Mount Sinai Medical Center
- Us TOO

Thank You!

You will receive two emails after the summit:

1. **A survey** to share your feedback on the summit as well as insights into future programming.

2. **Information** from the Summit day, including this presentation and instructions on how to use our Clinical Trial Finder service.



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