<table>
<thead>
<tr>
<th>Scientific Experts</th>
<th>Patient Experts</th>
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<tbody>
<tr>
<td><strong>David A. Reardon, M.D.</strong></td>
<td><strong>Ernestina Dos Reis</strong></td>
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<tr>
<td>Dana-Farber Cancer Institute</td>
<td>Glioblastoma</td>
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<tr>
<td><strong>Susanne Baumeister, M.D.</strong></td>
<td><strong>Ariella Chivil</strong></td>
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<tr>
<td>Boston Children’s Hospital</td>
<td>Hodgkin Lymphoma</td>
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<tr>
<td><strong>Justin F. Gainor, M.D.</strong></td>
<td><strong>Cole Malone</strong></td>
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<tr>
<td>Massachusetts General Hospital</td>
<td>Acute Lymphoblastic Leukemia</td>
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<td><strong>Kimmie Ng, M.D.</strong></td>
<td><strong>Denise Malone</strong></td>
</tr>
<tr>
<td>Dana-Farber Cancer Institute</td>
<td>Cole’s mother and caregiver</td>
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<td></td>
<td><strong>John White</strong></td>
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<td>Prostate Cancer</td>
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This event is made possible with generous support from:

- Bristol-Myers Squibb
- Merck
- Genentech
- GSK
- Lilly Oncology
- Immunotherapy Foundation
- Regeneron
- Sanofi Genzyme
- Novartis
- Pfizer
Our Educational Partners

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- Patient Empowerment Network
- The Jimmy Fund
- Us TOO
- Wellness Warriors Boston
- Young Survival Coalition
### Schedule of Events

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>9:00 am</td>
<td>Registration and networking</td>
</tr>
<tr>
<td>10:00 am</td>
<td>Program commences</td>
</tr>
<tr>
<td>10:15 am</td>
<td><strong>WELCOME</strong>&lt;br&gt;David A. Reardon, M.D.</td>
</tr>
<tr>
<td>10:30 am</td>
<td><strong>HEAR FROM THE EXPERTS</strong>&lt;br&gt;Immunotherapy Basics&lt;br&gt;David A. Reardon, M.D.</td>
</tr>
<tr>
<td>11:00 am</td>
<td><strong>PANEL: RESEARCH UPDATES</strong>&lt;br&gt;Panelists&lt;br&gt;Susanne Baumeister, M.D.&lt;br&gt;Justin F. Gainor, M.D.&lt;br&gt;Kimmie Ng, M.D., M.P.H.</td>
</tr>
<tr>
<td>11:30 am</td>
<td><strong>PATIENT PERSPECTIVE</strong>&lt;br&gt;A message from Ariella Chivil, Hodgkin lymphoma survivor</td>
</tr>
<tr>
<td>12:00 pm</td>
<td>Lunch and networking</td>
</tr>
<tr>
<td>1:00 pm</td>
<td><strong>LEARN ABOUT CLINICAL TRIALS</strong>&lt;br&gt;Brian Brewer</td>
</tr>
<tr>
<td>1:30 pm</td>
<td><strong>IMMUNOTHERAPY PATIENT PANEL</strong>&lt;br&gt;Panelists&lt;br&gt;Ernestina Dos Reis&lt;br&gt;Cole Malone&lt;br&gt;Denise Malone&lt;br&gt;John White</td>
</tr>
<tr>
<td>2:00 pm</td>
<td>Transitional Break</td>
</tr>
<tr>
<td>2:15 pm</td>
<td><strong>BREAKOUT SESSIONS</strong>&lt;br&gt;Your choice of moderated, deeper-dive Q&amp;A with our experts&lt;br&gt;<strong>General Immunotherapy</strong>&lt;br&gt;David A. Reardon, M.D.&lt;br&gt;<strong>Childhood Cancer</strong>&lt;br&gt;Susanne Baumeister, M.D.&lt;br&gt;<strong>Gastrointestinal Cancer</strong>&lt;br&gt;Kimmie Ng, M.D., M.P.H.&lt;br&gt;<strong>Lung and Esophageal Cancers</strong>&lt;br&gt;Justin F. Gainor, M.D.</td>
</tr>
<tr>
<td>3:15 pm</td>
<td>Program closes</td>
</tr>
<tr>
<td>9:00 am – 4:00 pm</td>
<td><strong>CLINICAL TRIAL NAVIGATOR APPOINTMENTS</strong>&lt;br&gt;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.</td>
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After the Summit

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](#).
Welcome

Laurie H. Glimcher, M.D.
President and CEO, Dana-Farber Cancer Institute
Richard and Susan Smith Professor of Medicine,
Harvard Medical School
Overview

A. Background

B. Basics: How our immune system works
   - Immune checkpoint therapy
   - Adoptive cellular therapies, CARS
   - Oncolytic viruses
   - Vaccines

C. Challenges
Origin & Revival of Immunotherapy

1890s: William B. Coley
1900s: Paul Ehrlich
1960s: Lloyd J. Old
Attributes of our Immune System

1. Highly potent, coordinated attack

2. Exquisite specificity: designed to avoid cross-reactivity and damage to normal cells

3. Memory

**Faroe Islands**
- 1781: measles outbreak
- 1846: 2nd outbreak

*No one infected in 1st outbreak got measles with 2nd outbreak*
Immunotherapy: A Potential Cure?

Standard therapy:
- Pts take longer to progress, but succumb at the same rate.

Immunotherapy:
- Increased survival.
- Room for improvement.
The Immune System at a Glance: Our Natural Defense System

**Nose**
Hairs and mucus trap foreign particles and prevent them from entering the body.

**Thymus**
Small organ located just behind the breastbone where T cells mature (the “T” is for thymus).

**Bone marrow**
Tissue in the center of bones that is responsible for making blood cells, including white blood cells.

**Tonsils**
Structures at the back of the throat that sample bacteria and viruses that enter the body through the mouth or nose.

**Lymph nodes**
Small, bean-shaped structures located throughout the body that filter lymph fluid, where immune cells are alerted to the presence of pathogens or cancer.

**Spleen**
Flat-sized organ located in the upper-left part of the abdomen, containing white blood cells that fight infection and cancer.

**White blood cells**
White blood cells— including macrophages, dendritic cells, and lymphocytes—are the cellular actors of immunity.

**Lymphatic vessels**
Thin-walled tubes that collect and transport lymph fluid throughout the body.
The Cells of the Immune System: The “Soldiers” in our Army

- Dendritic Cell
- Monocyte
- Neutrophil
- B Cell
- Natural Killer Cell
- Macrophage
- T Cell
Adaptive Immune Responses Against Cancer

Cancer Cell (being engulfed)

Antigen-Presenting Cell (e.g., Dendritic Cell)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

Tumor Antigens
Adaptive Immune Responses Against Cancer

Tumor Antigen (bound by MHC1)

Antigen-Presenting Cell (e.g., Dendritic Cell)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

Tumor Antigen (bound by MHC1)

T Cell Receptor (TCR)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

ACTIVATED “KILLER” T CELL
Activated "killer" T Cell

Cancer Cell
Adaptive Immune Responses Against Cancer

Cancer Cell  Activated “killer” T Cell
Adaptive Immune Responses Against Cancer

CANCER CELL ELIMINATED!
Activated "killer" T Cell

PDL1 - PD1

Immune Checkpoints Can Suppress Immune Responses
Immune Checkpoints Can Suppress Immune Responses

Cancer Cell

Activated “killer” T Cell

PDL1- PD1
Immune Checkpoints Can Suppress Immune Responses

Normally, PDL1-PD1 leads to T cell “exhaustion”
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell

PD-1/PD-L1 Checkpoint Inhibitors
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell

PD-1/PD-L1 Pathway Blocked!
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell

CANCER CELL ELIMINATED!
Adoptive T Cell Immunotherapy

1. Isolation
2. Activation
3. Expansion
4. Re-infusion
Adoptive T Cells In Action (Against Melanoma)

Melanoma (Before)

Melanoma (After)
T Cell Receptor Engineering

Equip T cells with new, cancer-targeting TCR
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
CAR T Cell Immunotherapy
(Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
• Viruses can alter our cells’ DNA, by inserting their own genetic material
• Impaired defenses make tumor cells more susceptible to infection
AFTER INJECTION:

1) Viruses cause tumor cells to “burst” & release antigens
2) Immune cells uptake & present tumor antigens
3) Stimulates adaptive, and potentially systemic, immune responses
Reprogramming Oncolytic Viruses To Enhance Anti-Tumor Activity

(+) INSERT Immune-stimulating genes

(—) REMOVE Disease-causing genes (selective targeting of tumors)
Cancer Vaccines

Tumor Antigens
(provided by vaccine)
Cancer Vaccines

Dendritic cell
Cancer Vaccines
Cancer Vaccines

Dendritic cell

ACTIVATED “KILLER” T CELL
Vaccine-Induced Elimination of Cancer Cells

Cancer Cell

Activated “killer” T Cell
Vaccine-Induced Elimination of Cancer Cells

Cancer Cell  Activated “killer” T Cell
Personalized Neoantigen Vaccine Trial
Challenges in Cancer Immunotherapy

• Discovering and validating new biomarkers to help doctors predict which patients will respond to which immunotherapies

• Determining the best way to combine immunotherapies with each other as well other treatments to extend immunotherapy’s benefits for more patients

• Learning how to decouple side effects of immunotherapy from benefit
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells

2. Cancers secrete chemicals to turn off the immune system
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells

2. Cancers secrete chemicals to turn off the immune system

3. Cancers recruit suppressive cells to inactivate/block the immune response
Immunotherapy 101

Conclusion

A. Background

B. Basics: How our immune system works
   - Immune checkpoint therapy
   - Adoptive cellular therapies, CARS
   - Oncolytic viruses
   - Vaccines

C. Challenges
Panel Discussion

LATEST RESEARCH UPDATES

Panelist
Susanne Baumeister, M.D.
Childhood cancer

Panelist
Justin Gainor, M.D.
Esophageal and lung cancers

Panelist
Kimmie Ng, M.D., M.P.H.
Gastrointestinal cancer

Moderator
David A. Reardon, M.D.
Neurological cancer
Patient Perspective

Ariella Chivil
Surviving Hodgkin Lymphoma
Lunch and Networking
Lavine Family Dining Pavilion
Brian Brewer
Cancer Research Institute

LEARN ABOUT CLINICAL TRIALS
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
Getting from Discovery to Approval

- Drug Discovery
  - 3 - 6 years
  - ~5,000-10,000 compounds

- Preclinical
  - 250

- Clinical Trials
  - 5
  - Phase 1
    - 20-100
  - Phase 2
    - 100-500
  - Phase 3
    - 1,000-5,000
  - 6 - 7 years

- FDA Review
  - 0.5 - 2 years

- Scale-Up to Mfg.
  - INDEFINITE

- Post-Marketing Surveillance

Source: AppliedClinicalTrials.com

CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY PATIENT SUMMIT
What Are Clinical Trial Phases?

**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+

# Pros and Cons of Clinical Trials

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

*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 will 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?
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
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.

Clinical Trials: Myth versus Fact

**MYTH**

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

**FACT**

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

Clinical Trials: Myth versus Fact

**MYTH**

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

**FACT**

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

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

**MYTH**

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

**FACT**

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

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

**MYTH**

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

**FACT**

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

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

MYTH

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

FACT

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.

Clinical Trials: Myth versus Fact

**MYTH**

Clinical trials aren’t safe.

**FACT**

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

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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BREAKOUT SESSIONS
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Boston July 29, 2019