Cancer Research Institute
Immunotherapy Patient Summit
San Francisco • Chicago • New York • Houston • Tampa

Houston January 27, 2018
Brian Brewer
Cancer Research Institute

WELCOME
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Thank you to those who helped promote the summit

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Coalition for Clinical Trial Awareness  Immunotherapy Foundation
Colon Cancer Alliance  Let Life Happen
Dan L Duncan Comprehensive Cancer Center  Melanoma Research Foundation
Fight Colorectal Cancer  MD Anderson Cancer Center
Focused Ultrasound Foundation  National Ovarian Cancer Coalition
FORCE  Patient Empowerment Network
GI Cancers Alliance  Survivors Offering Support Sugarland
US TOO
Our Guest Faculty

Scientific Experts

Charles Drake, M.D., Ph.D.
Columbia University Medical Center

Carlos Ramos, M.D., Ph.D.
Baylor College of Medicine

Andrew Sikora, M.D., Ph.D.
Baylor College of Medicine

Sumit Subudhi, M.D., Ph.D.
MD Anderson Cancer Center

Jun Zhang, M.D.
Baylor College of Medicine

Patient Experts

Dale Biggs
Squamous Cell Carcinoma

Katherine (K.C.) Dill
Lung Cancer

Janie Ferling
Melanoma

Adam Requena
Mesothelioma
# Schedule of Events

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00am</td>
<td>Registration and networking</td>
</tr>
<tr>
<td>10:00am</td>
<td>Program commences</td>
</tr>
<tr>
<td></td>
<td><strong>Welcome</strong></td>
</tr>
<tr>
<td></td>
<td>Brian Brewer</td>
</tr>
<tr>
<td>10:15am</td>
<td><strong>Hear from the experts</strong></td>
</tr>
<tr>
<td></td>
<td>Learn the basics of immunotherapy</td>
</tr>
<tr>
<td></td>
<td>Charles Drake, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Latest research update panel</td>
</tr>
<tr>
<td></td>
<td><strong>Moderator</strong></td>
</tr>
<tr>
<td></td>
<td>Charles Drake, M.D., Ph.D.</td>
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<tr>
<td></td>
<td><strong>Panelists</strong></td>
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<tr>
<td></td>
<td>Carlos Ramos, M.D., Ph.D.</td>
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<tr>
<td></td>
<td>Andrew Sikora, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td>Sumit Subudhi, M.D., Ph.D.</td>
</tr>
<tr>
<td>11:30am</td>
<td><strong>Patient perspective</strong></td>
</tr>
<tr>
<td></td>
<td>Hear from a melanoma survivor</td>
</tr>
<tr>
<td></td>
<td>Janie Ferling</td>
</tr>
<tr>
<td>1:00pm</td>
<td><strong>Demystifying clinical trials</strong></td>
</tr>
<tr>
<td></td>
<td>Learn about clinical trials and panel discussion</td>
</tr>
<tr>
<td></td>
<td><strong>Moderator</strong></td>
</tr>
<tr>
<td></td>
<td>Brian Brewer</td>
</tr>
<tr>
<td></td>
<td><strong>Panelists</strong></td>
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<tr>
<td></td>
<td>Dale Biggs</td>
</tr>
<tr>
<td></td>
<td>Katherine Dill</td>
</tr>
<tr>
<td></td>
<td>Adam Requena</td>
</tr>
<tr>
<td>2:00pm</td>
<td>Beverage break</td>
</tr>
<tr>
<td>2:15pm</td>
<td><strong>Breakout sessions</strong></td>
</tr>
<tr>
<td></td>
<td>Your choice of moderated discussion with our experts or a general networking session</td>
</tr>
<tr>
<td></td>
<td><strong>Urologic Cancer</strong></td>
</tr>
<tr>
<td></td>
<td>Sumit Subudhi, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td><strong>Head and Neck Cancer</strong></td>
</tr>
<tr>
<td></td>
<td>Andrew Sikora, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td><strong>Blood Cancer and HPV-Associated Cancers</strong></td>
</tr>
<tr>
<td></td>
<td>Charles Drake, M.D., Ph.D.</td>
</tr>
<tr>
<td></td>
<td><strong>General Immunotherapy &amp; Networking</strong></td>
</tr>
<tr>
<td></td>
<td>Charles Drake, M.D., Ph.D.</td>
</tr>
<tr>
<td>3:15pm</td>
<td>Program closes</td>
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<tr>
<td>9:00am - 4:00pm</td>
<td><strong>Clinical trial navigator appointments</strong></td>
</tr>
<tr>
<td></td>
<td>Appointments will be available all day. If you didn’t pre-register, check with the registration desk</td>
</tr>
</tbody>
</table>
Charles Drake, M.D., Ph.D.
Director GU Medical Oncology
Co-Director Immunotherapy Program
Associate Director for Clinical Research
Professor of Oncology
Herbert Irving Cancer Center at Columbia University

IMMUNOTHERAPY BASICS
T Cells
Activating T Cells In Tumors
Activating T Cells Outside of Tumors
Combination Immunotherapy
CD8 T Cells Are Born to Kill
Killer T Cells in Tumors

Brown Staining = CD8 T Cells
Why Are Those Killer T Cells Not Killing?

CD8 T Cells are Being Held in Check (Exhausted) WHEN PD-L1 is Expressed
Blocking PD-1 (or PD-L1) Allows T Cells to Regain the Capacity to Kill

“Exhausted” Tumor Infiltrating T Cell
Rapid Tumor Shrinkage (in some patients)
Evidence of Killing

Vol 31, No 15_suppl (May 20 Supplement), 2013: 4514 ASCO 2013
Blocking PD-1 (or PD-L1) Allows T Cells to Proliferate

Anti-PD-1 or Anti-PD-L1

“Exhausted” Tumor Infiltrating T Cell
Temporary Tumor Growth Before Shrinking
Evidence of T Cell Proliferation in Patients
Long Term Responses Off Treatment
Evidence for T Cell Memory?

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
January First treatment
March 2 month evaluation

2010: Complete Response

- Patient received 3 study treatments
- Limited side effects
- Rapid treatment response
- Cancer-free for 8+ years
Other Approaches

Brown Staining = CD8 T Cells
MORE T Cells = Better Adoptive Transfer

T cells isolated from patient

T Cells Expanded And Activated

T Cells Re-Infused
BETTER T Cells = Better Chimeric Antigen Receptor T Cells (CAR-T)

Natural T Cell Receptor

Chimeric Antigen Receptor

High Affinity Tumor binding domain

Signaling domain

Courtesy of Carl June, U Penn
In Girl’s Last Hope, Altered Immune Cells Beat Leukemia

By DENISE GRADY  DEC. 9, 2012

Emma Whitehead, with her mother, Karl. 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
Not All Tumors Have T Cells: Combination Approaches

Kidney Tumor with T Cells  
Kidney Tumor

Brown Staining = CD8
The Tumor Microenvironment is a VERY Unfriendly Place

**Suppressive Factors**

- **CD8 T cell**: TCR, MHC, CTLA-4
- **Regulatory CD4 T Cell (FoxP3+)**: CTLA-4
- **Tumor cell**: MHC

**Anti-CTLA-4**

CTLA-4 is upregulated in regulatory T cells and tumor cells, leading to T-cell suppression. Anti-CTLA-4 therapies aim to restore T-cell function and improve immune responses against tumors.
Combining Two Immunotherapies (Anti-PD-1 and Anti-CTLA-4) Can Sometimes Increase Toxicity

<table>
<thead>
<tr>
<th>Event</th>
<th>Cohort 1 (N=14)</th>
<th>Cohort 2 (N=17)</th>
<th>Cohort 2a (N=10)</th>
<th>Cohort 3 (N=8)</th>
<th>All Patients in Concurrent Regimen Group (N=33)</th>
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<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>Grade 3 or 4</td>
<td>All Grades</td>
<td>Grade 3 or 4</td>
<td>All Grades</td>
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<tr>
<td></td>
<td>Number of Patients</td>
<td>Percentage</td>
<td>Number of Patients</td>
<td>Percentage</td>
<td>Number of Patients</td>
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<td>Pneumonitis</td>
<td>1 (7)</td>
<td>0</td>
<td>2 (13)</td>
<td>1 (6)</td>
<td>0</td>
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<tr>
<td>Endocrinopathy</td>
<td>1 (7)</td>
<td>0</td>
<td>3 (18)</td>
<td>1 (6)</td>
<td>2 (13)</td>
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<td>Hypothyroidism</td>
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<td>0</td>
<td>2 (12)</td>
<td>0</td>
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<tr>
<td>Hypophyisis</td>
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<td>0</td>
<td>1 (6)</td>
<td>0</td>
<td>1 (17)</td>
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<tr>
<td>Thyroiditis</td>
<td>0</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
<td>1 (17)</td>
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<tr>
<td>Adrenal insufficiency</td>
<td>0</td>
<td>0</td>
<td>2 (12)</td>
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<tr>
<td>Hyperthyroidism</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
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<td>1 (17)</td>
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<tr>
<td>Thyroid-function results abnormal</td>
<td>1 (7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (2)</td>
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<tr>
<td>Hepatic disorder</td>
<td>4 (29)</td>
<td>3 (21)</td>
<td>5 (29)</td>
<td>3 (18)</td>
<td>2 (13)</td>
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<tr>
<td>Asparagin transferase increased</td>
<td>4 (29)</td>
<td>3 (21)</td>
<td>4 (24)</td>
<td>2 (12)</td>
<td>2 (13)</td>
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<tr>
<td>Alanine aminotransferase increased</td>
<td>3 (21)</td>
<td>2 (14)</td>
<td>5 (29)</td>
<td>3 (18)</td>
<td>2 (13)</td>
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<tr>
<td>Gastrointestinal disorder</td>
<td>5 (36)</td>
<td>1 (7)</td>
<td>6 (35)</td>
<td>2 (12)</td>
<td>6 (38)</td>
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<tr>
<td>Diarrhea</td>
<td>5 (36)</td>
<td>0</td>
<td>5 (29)</td>
<td>1 (6)</td>
<td>5 (31)</td>
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<tr>
<td>Colitis</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>2 (13)</td>
<td>1 (6)</td>
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<tr>
<td>Renal disorder</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>1 (6)</td>
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<tr>
<td></td>
<td>Blood creatinine increased</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>1 (6)</td>
<td>1 (6)</td>
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<tr>
<td>Acute renal failure</td>
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<td>1 (6)</td>
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<tr>
<td>Renal failure</td>
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<td>0</td>
<td>1 (6)</td>
<td>1 (6)</td>
<td>0</td>
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<tr>
<td>Tubulointerstitial nephritis</td>
<td>1 (7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Skin disorder</td>
<td>10 (71)</td>
<td>1 (7)</td>
<td>14 (82)</td>
<td>1 (6)</td>
<td>1 (6)</td>
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<tr>
<td>Rash</td>
<td>8 (57)</td>
<td>1 (7)</td>
<td>11 (65)</td>
<td>0</td>
<td>7 (44)</td>
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<tr>
<td>Pruritus</td>
<td>6 (43)</td>
<td>0</td>
<td>11 (65)</td>
<td>0</td>
<td>7 (44)</td>
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<tr>
<td>Urticaria</td>
<td>0</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Blister</td>
<td>0</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*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 Medicinal 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 1 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.
Combination Immunotherapy Can Be VERY Active

Other Ways Tumors Resist the Immune System

IDO

- Breaks down tryptophan
- Tryptophan is essential for T cell function
Combining T Cell Re-Activation (anti-PD-1) With IDO Inhibition
Our Challenge

Targets on T Cells

Targets in the Tumor Microenvironment

- IDO
- Adenosine / A2A Receptor
- TGF-Beta
- Interleukin 8
- CSF-1
- NLRP3
Additional Information:
Useful resources about cancer immunotherapy

https://www.cancerresearch.org/patients/what-is-immunotherapy

https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html

https://www.cancer.gov/research/areas/treatment/immunotherapy-using-immune-system

https://www.mdanderson.org/treatment-options/immunotherapy.html

https://www.pennmedicine.org/cancer/navigating-cancer-care/treatment-types/immunotherapy
Panel Discussion

LATEST RESEARCH UPDATE
Scientific Panel

Moderator
Charles Drake, M.D., Ph.D.

Panel
Carlos Ramos, M.D., Ph.D.
Blood Cancer & HPV-Associated Cancers
Andrew Sikora, M.D., Ph.D.
Head and Neck Cancer
Sumit Subudhi, M.D., Ph.D.
Urologic Cancer
Janie Ferling
Melanoma Survivor

PATIENT PERSPECTIVE
LUNCH AND NETWORKING
DEMYSTIFYING CLINICAL TRIALS

Brian Brewer
Cancer Research Institute
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

- Pre-Discovery: 3 - 6 years, ~5,000-10,000 compounds
- Drug Discovery
- Preclinical: 250
- Clinical Trials: 5 phases
- FDA Review: 0.5 - 2 years
- Scale-Up to Mfg.
- Post-Marketing Surveillance: indefinite
- Number of Volunteers:
  - Phase 1: 20-100
  - Phase 2: 100-500
  - Phase 3: 1,000-5,000

Source: AppliedClinicalTrials.com
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>

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?

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.

Fact: Placebos are rarely used and never given in the absence of some form of treatment.
Clinical Trials: Myth versus Fact

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.

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.
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.
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.

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.

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.

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/
Panel Discussion

IMMUNOTHERAPY CLINICAL TRIALS
Patient Panel

Moderator
Brian Brewer

Panel
Dale Biggs
Squamous Cell Carcinoma
Katherine (K.C.) Dill
Lung Cancer
Adam Requena
Mesothelioma
BREAKOUT SESSIONS
<table>
<thead>
<tr>
<th>Breakout Rooms</th>
<th>Location</th>
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<tbody>
<tr>
<td><strong>Blood Cancer &amp; HPV-Associated Cancers</strong></td>
<td>N317</td>
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<tr>
<td>Carlos Ramos, M.D., Ph.D.</td>
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<td><strong>Head and Neck Cancer</strong></td>
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<tr>
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<td>McMillian</td>
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<tr>
<td>Sumit Subudhi, M.D., Ph.D.</td>
<td></td>
</tr>
<tr>
<td><strong>General Immunotherapy</strong></td>
<td>Kleberg (Here)</td>
</tr>
<tr>
<td>Charles Drake, M.D., Ph.D.</td>
<td></td>
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IMMUNOTHERAPY PATIENT SUMMIT

San Francisco • Chicago • New York • Houston • Tampa

Houston January 27, 2018