Year-End Message from the Director

I have been the Director for the Abramson Cancer Center for six months, and I can already say it has been the most remarkable experience of my career—a “dream job” and a privilege.

As a physician-scientist here at Penn for 16 years, I knew from experience how remarkable our research faculty and staff are, and how amazingly dedicated the clinical teams are to our patients. Seeing all of this from a new vantage point, I am even more impressed and humbled by the quality of the Cancer Center’s people. For all you do, thank you sincerely.

In this brief period, we’ve seen the results of many long-term projects by ACC members that were taken up under Chi Dang’s leadership. We are all familiar with and incredibly proud of the work of Carl June, Stephan Grupp, David Porter, Bruce Levine, and the hundreds of colleagues, technical, and clinical staff that led to the FDA approval of Kymriah™ in August. Our CAR-T Flashmob was a team event to remember! Our Penn and CHOP colleagues are not resting on their laurels, and you’ll read in this issue about Stephen Schuster’s CAR T cell therapy breakthrough results in a global trial for Non-Hodgkin’s Lymphoma, in addition to advances in CAR T cell treatments for myeloma, multiple myeloma, and B-cell ALL.

ACC members continue to publish in the most impressive journals such as Nature and its sister journals, as well as NEJM, Science, Cancer Discovery, JAMA, and Cell.

More accomplishments are on the horizon. John Maris and Celeste Simon were named NCI Outstanding Scholars and received R35 grants. Carl June has a new P01 for CAR T cells in hematologic malignancies. David Mankoff and Joel Karp received an NCI Cancer Moonshot R33 for glutamine imaging using PET. Jim Metz and his team in Radiation Oncology opened a first-in-the-world radiation platform. Innovative initiatives in our PCAM clinic from Nursing, Pharmacy and the Cancer Service Line have been ground-breaking for our patients (thank you Lindsey Zinck, Suzanne McGettigan, Jennifer Braun, and Abbey Owens!). Shelley Berger and John Wherry have just received a $7M grant through the Penn/Celgene partnership (thank you Pat Morin!). Ron DeMatteo, a world-renowned surgical oncologist and researcher, joined Penn as Chair of Surgery. The Penn Veterinary Cancer Center, with its research focus on comparative oncology, opened under the leadership of Ellen Puré; and Nicola Mason of the School of Veterinary Medicine received an NCI U24 for canine immunotherapy trials. We’re looking forward to further opportunities as we set our sights on the new series of NCI Cancer Moonshot grants. Thank you especially to our teams in Development, Marketing and Communications – our national profile is higher than ever!

Our people were recognized for their accomplishments. Lewis Chodosh was elected to the National Association of Medicine. Hongzhe Li and Anil Rustgi were named AAAS fellows. Penn’s RadVax team was featured in the NCI’s 2019 annual budget plan and budget proposal. Four ACC faculty received major annual awards from the Perelman School of Medicine.

To echo former Vice President Joe Biden, when he kicked off the NCI Cancer Moonshot program here at Penn in 2016, we are at an inflection point in cancer research. We are now in the Era of Cancer Ecology. I cannot express how proud I am to be the ACC Director at such an incredible time, and to work with such amazing people.

Thank you all.

I wish you the joys of the holiday season, and look forward with all of you to a glorious and successful New Year.

Robert H. Vonderheide, MD, DPhil
Director, Abramson Cancer Center
Penn Presents New Data from Global CAR T Therapy Trials

In a pair of clinical trials stretching from Philadelphia to Tokyo, the chimeric antigen receptor (CAR) T cell therapy Kymriah™ (formerly known as CTL019) demonstrated long-lasting remissions in non-Hodgkin’s lymphoma (NHL) patients. Results from a global, multisite trial were presented at the 59th American Society of Hematology Annual Meeting and Exposition in Atlanta (Abstract #577). Results from the single-site study, with follow-up extending past two years, were published in the New England Journal of Medicine. Both studies were led by Stephen J. Schuster, MD, from the Abramson Cancer Center and the Perelman School of Medicine at the University of Pennsylvania.

In the global, multi-center, Novartis-sponsored trial known as JULIET, 40 percent of patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL), the most common form of NHL, who received the investigational treatment had a partial or complete response at three months. About 74 percent of patients who responded remained cancer-free at six months. The trial included 27 sites in 10 countries across North America, Europe, Australia, and Asia. In total, 81 patients were infused with CAR T cells and evaluated for a response. At three months, 26 patients (32 percent) achieved a complete response, while five (6 percent) achieved a partial response.

The research team says the updated results from an earlier study, of patients treated at the single-site pilot trial after their cancers had come back following standard treatments, 43 percent of DLBCL patients achieved complete remission, as did 71 percent of patients with follicular lymphoma, the second most common form of the disease. All patients who were in remission at six months are still in remission, after a median follow-up of 28.6 months.

“Taken together, our data from both trials show that most patients who are in remission at three months stay in remission,” said Schuster, who is the Robert and Margarita Louis-Dreyfus Professor in Chronic Lymphocytic Leukemia and Lymphoma Clinical Care and Research in the Perelman School of Medicine and director of the Lymphoma Program at the Abramson Cancer Center.

Carl June, MD, the Richard W. Vague Professor in Immunotherapy, director of the Center for Cellular Immunotherapies, and director of the Parker Institute for Cancer Immunotherapy at Penn, is the senior author on the single-site study.

Two-thirds of DLBCL cases are successfully treated with frontline chemotherapy. When that fails, a high-dose chemotherapy combined with an autologous stem cell transplant can potentially lead to long-term disease-free survival. But only half of these relapsed/refractory patients are candidates for this approach, and for those who are, the expected three-year event-free survival rate is just 20 percent in the current era of frontline immunotherapy. Follicular lymphoma can usually be treated with frontline chemotherapy, although 20 percent of patients relapse within two years. These patients have a five-year overall survival rate of just 50 percent using currently available therapies.

“About a third of patients who fail all current therapies, even transplant, could now have a form of therapy that may offer them durable remissions,” Schuster said. “This therapy has the potential to save lives if approved by the FDA for this indication.”

Kymriah™ was approved by the U.S. Food and Drug Administration in August 2017 for the treatment of patients up to 25 years of age with acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. Penn and Novartis formed a global research and development collaboration in 2012, the result of which was the first therapy based on gene transfer approved by the FDA. Results from JULIET served as the basis for a recent application submitted by Novartis to the FDA for approval of CTL019 for the treatment of adult patients with relapsed or refractory DLBCL who are ineligible for or relapse after autologous stem cell transplant (ASCT). Novartis is also seeking approval from the European Medicines Agency (EMA) for CTL019 in pediatric and young adult patients with relapsed or refractory B-cell ALL and adult patients with relapsed or refractory DLBCL who are ineligible for ASCT.

The treatment modifies patients’ own immune T cells, which are collected and reprogrammed to potentially seek and destroy the patients’ cancer cells. After being infused back into patients’ bodies, these newly built “hunter” cells both multiply

(Continued on page 3)
Seminars and So Forth

Monday 12/18/17 11:00 am
IRM Faculty Candidate Seminar
“Understanding the roles of onco-fetal programs during development and oncogenesis.” Jihan Osborne, Ph.D., Postdoctoral Fellow, Boston Children’s Hospital, Harvard Medical School
Room 251 BRB II/III

Monday 12/18/17 12:00 pm
Epigenetics Distinguished Seminar
“The dynamic epitranscriptome: Control of mRNA and lncRNA by RNA modification.” Samie R. Jaffrey, MD, PhD, Greenberg-Starr Professor, Pharmacology, Weill Medical College, Cornell University
CRB Austrian Auditorium

Tuesday 12/19/17 12:00 pm
Division of Medical Ethics Invited Speaker
“Curiosity, Confrontation, and Collaboration: truth-telling in the multicultural context.” Abby R. Rosenberg, MD, MS, MA, Assistant Professor, Pediatrics, University of Washington School of Medicine; Attending Physician, Cancer and Blood Disorders Center, Seattle Children’s Hospital
1402 Blockley Hall

Tuesday 12/19/17 4:00 pm
CHOP CCCR Oncology Seminar Series
“Promoting Resilience in Children and Families Facing Serious Pediatric Illness.” Abby R. Rosenberg, MD, MS, Medical Director, Adolescent and Young Adult Oncology, Cancer and Blood Center; Assistant Professor, Divisions of Hematology-Oncology and Bioethics, Seattle Children’s Hosp.
CTRB 1200A (CHOP)

Tuesday 12/19/17 4:00 pm
Immunology Colloquium
“Allogenicity in Transplantation and Regenerative Cell Therapy.” Dominique Charron, MD, PhD, Professor Emeritus of Immunology, Université Paris - Diderot
CRB Austrian Auditorium

Thursday 12/21/17 9:00 am
Gastroenterology Research Seminar
“The Intestinal Stem Cell Niche - The Final Answer.” Klaus Kaestner, PhD, Thomas and Evelyn Suor Butterworth Professor in Genetics, PSOM
901 Blockley Hall

New Data From Global CAR T Cell Trials

(Continued from page 2)
and attack, targeting cells that express a protein called CD19. Tests reveal that the army of hunter cells can grow to more than 10,000 new cells for each single engineered cell patients receive, producing high remission rates. They can also survive in the body for years. CTL019 uses the 4-1BB costimulatory domain in its chimeric antigen receptor to enhance cellular expansion and persistence.

Cytokine-release syndrome (CRS), a toxicity associated with CAR T therapy which includes varying degrees of flu-like symptoms, with high fevers, nausea, and muscle pain, and can require ICU-level care, was reported in 58 percent of the patients in multi-site study. Fifteen of those patients (26 percent) required treatment with tocilizumab, which is the standard therapy for the toxicity. All of those patients recovered from their CRS. Other toxicities included infections (34 percent of patients), cytopenias or low blood count (36 percent), neurologic events (21 percent), febrile neutropenia (13 percent), and a metabolic abnormality called tumor lysis syndrome (one percent). All of the toxicities resolved on their own or with treatment, and there were no treatment-related deaths.

In the single-site trial, CRS was reported in five patients. Only one of those patients required treatment with tocilizumab. That patient recovered and achieved a complete response. Eleven patients reported temporary neurologic symptoms, including delirium. Ten of the 11 cases were self-limited and resolved without ICU care. The 11th case resolved after treatment.

The ACC presented multiple other CAR T studies at the ASH Meeting that look beyond CTL019, including:

- Using CART-BCMA, a specifically engineered type of CAR T cell, to target multiple myeloma. (Cohen, Abstract #505)
- Manufacturing anti-CD22 CAR T cells for B-cell acute lymphoblastic leukemia (Gill, Abstract #807)
- Using a different kind of T cell to treat myeloma, NY-ESO-1 SPEAR T-cells (Stadtmauer, Abstract #845)

Further Reading
ASH 59th Annual Meeting Abstracts
Credit: Penn Medicine Communications
"In the few short years that I have worked with the Abramson Cancer Center, I have seen it lead transformative changes in the treatment of cancer. I know that ACC could not have achieved as great an impact without philanthropic support. I give to ACC because I would like ACC to continue to reduce the cancer burden in our world."

- Carmen E. Guerra, M.D., M.S.C.E., F.A.C.P.
  Associate Professor of Medicine
  Vice Chair of Diversity and Inclusion, Department of Medicine
  Associate Director of Diversity and Outreach, Abramson Cancer Center

---

**Funding Opportunities**


The purpose of these FOAs is to: identify new, information technology (IT)-enabled delivery models that support systematic screening and treatment of depression in cancer patients; test the feasibility of implementing these new delivery models in a variety of oncology practice settings, especially those serving under-served populations; and test the usability and potential effectiveness of the IT-specific components of these new delivery models.


**PA-18-476/PA-18-477 Cancer Research Education Grants Program (R25)**


The over-arching goal of this NCI R25 program is to support educational activities that complement and/or enhance the training of a workforce to meet the nation’s biomedical, behavioral and clinical research needs.

These FOAs will support creative educational activities with a primary focus on Curriculum or Methods Development (PA-18-476) or Courses for Skills Development (PA-18-477). Applications are encouraged that propose innovative, state-of-the-art programs that address the cause, diagnosis, prevention, or treatment of cancer, rehabilitation from cancer, or the continuing care of cancer patients and the families of cancer patients.


**PAR-18-467/PAR-18-466 NCI Transition Career Development Award (K22)**


These FOAs support an NCI program that facilitates the transition of investigators in mentored, non-independent cancer research positions to independent faculty cancer research positions. This goal is achieved by providing protected time through salary and research support for the initial 3 years of the first independent tenure-track faculty position, or its equivalent, beginning at the time when the candidate starts a tenure-track faculty position.

**PAR-18-466** is designed specifically for applicants proposing to serve as the lead investigator of an independent clinical trial, a clinical trial feasibility study, or a separate ancillary study to an existing trial, as part of their research and career development. Applicants not planning an independent clinical trial, or proposing to gain research experience in a clinical trial led by another investigator, must apply to the companion FOA, **PAR-18-467**.


**PA-18-484 NIH Research Project Grant (R01)**


The NIH Research Project Grant supports a discrete, specified, circumscribed project in areas representing the specific interests and competencies of the investigator(s). The proposed project must be related to the programmatic interests of one or more of the participating NIH Institutes and Centers (ICs) based on their scientific missions.