65th Meeting of the National Cancer Institute (NCI) Director's Consumer Liaison Group (DCLG) Teleconference Summary

Public Location: NIH Campus, Building 31C, 6th Floor, Conference Room 10

Thursday, June 26, 2014

Members Present

Mr. Max Wallace, Chair
Mr. David Arons
Ms. Susan Braun
Dr. Adam Clark
Ms. Martha Gaines
Ms. Joya Delgado Harris
Ms. Linda House
Mr. Jeffrey Kaufman
Dr. Michelle McMurry-Heath
Mr. Jon Retzlaff
Mr. Josh Sommer
Dr. Regina Vidaver

Speakers

Ms. Anne Lubenow, Deputy Executive Officer, Office of Management, Office of the Director, NCI
Ms. Amy Bulman, Special Assistant to the Deputy Director, NCI
Dr. Jeffrey Abrams, Director for Clinical Research, Division of Cancer Treatment and Diagnosis, NCI
Dr. Christopher Heery, Director, Clinical Trials Group, Laboratory of Tumor Immunology and Biology and Medical Oncology Service, NCI
Mr. Jon Retzlaff, DCLG Member (Co-Chair of the DCLG Organizational Engagement Working Group)
Ms. Joya Delgado Harris, DCLG Member (Co-Chair of the DCLG Advocate Engagement Working Group)
Mr. Max Wallace, DCLG Chair and Chair of the Informed Consent Working Group)

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Welcome and Opening Remarks
Ms. Anne Lubenow

- Ms. Lubenow opened the teleconference, noting that Kelley Landy, acting director of NCI's Office of Advocacy Relations (OAR), planned to chair the meeting but had a family emergency.

- Ms. Lubenow reviewed conflict-of-interest policies and asked DCLG members to voluntarily abstain from participation in discussions that would involve a conflict for them because of financial or other interests.

- Dr. McMurry-Heath's term has ended with the DCLG, and two new members have joined: Dr. Regina Vidaver of the University of Wisconsin School of Medicine and Public Health and Ms. Mila McCurrach of the Lustgarten Foundation.

NCI's National Clinical Trials Network and Its New Precision Medicine Initiatives
Dr. Jeffrey Abrams

- Changes to clinical trials began in the late 1950s, when NCI launched the Clinical Trials Cooperative Group Program. Recent milestones have included the 2005 report of the Clinical Trials Working Group, which recommended a more efficient restructuring of trials, and the 2006 NCI Translational Research Working Group report, which included recommendations to improve translation of research results into clinical practice.

- In 2010, the NCI Clinical Trials and Translational Research Advisory Committee's Operational Efficiency Working Group (OEWG) released a report recommending accelerated timelines for trials, and the Institute of Medicine recommended reinvigorating the cooperative groups, including condensing and consolidating the nine adult cooperative groups.

- Since then, the groups have combined into four adult and one children's group, which are coordinated and funded by the National Clinical Trials Network (NCTN). Other networks, including the Community Clinical Oncology Programs, were incorporated into the NCI Community Oncology Research Program (NCORP).

- The new system is centralized and more efficient, with tumor banks for each group and a common data management system (Medidata Rave®). The base funding remains at $151 million, with reapportionment increasing the share for network lead academic sites that are participating, radiotherapy and imaging core service centers, and integrated translational science centers to use biomarkers and other leading diagnostic markers.

- An additional $70.2 million is designated for central institutional review boards (IRBs), a cancer trials support unit, tumor banks, NCORP treatment trials, and the Biomarker, Imaging and Quality of Life Studies Funding Program.

- NCI's national strategy for precision medicine includes advancing molecular profiling from research to the clinic, selecting patients based on molecular alterations, and developing a public database that links clinical outcomes with molecular tumor characteristics.

- The following trials to move from genotype to phenotype are underway: the Lung Cancer Master Protocol (LungMAP), a phase II/III study of therapies for second line squamous cell lung cancer; the Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST), a phase III study of adjuvant treatments for non-squamous non-small cell lung cancer (NSCLC); and the Molecular Analysis for Therapy Choice (NCI-MATCH) trial, a phase II study of solid tumors and lymphomas that have progressed after treatment.

Highlights from Questions and Answers

- NCTN projects are subject to peer review.

- Institutions are responding positively to central IRBs. They recognize that a central IRB has a greater ability to protect patients.

- In the new paradigm of cancer therapy, diagnostics are as important as treatment. The need for additional biopsies adds expense and will limit the number of trials, because each trial is more costly.

- NCORP has funding for psychosocial and similar support for patients in trials.

- Without additional funding, the number of patients in NCTN trials will gradually fall from the approximate 20,000 currently in cooperative group trials to about 17,000.

Cancer Immunotherapy Overview
Dr. Christopher Heery

- NCI asked Dr. Heery to present an overview and discussion of the history and future directions of cancer immunotherapy, which can serve as a primer for the October 2014 DCLG meeting.

- The field of oncology has only recently included the role of the immune system as a treatment modality.

- Early immunologic approaches included using Bacillus Calmette-Guérin (BCG) to treat bladder cancer in the 1970s, U.S. Food and Drug Administration (FDA) approval of a monoclonal antibody in 1986, and approval of interleukin-2 (IL-2) for treatment of renal

cell carcinoma in 1992. The FDA approved PROVENGE for treatment of metastatic prostate cancer in 2010, and ipilimumab for treatment of metastatic melanoma in 2011.

- PROVENGE has been a controversial treatment and critics have questioned whether it actually worked. The treatment is expensive and it is not clear that it prevents progression-free survival.

- Ipilimumab has marked a tectonic shift in the landscape of immunotherapy for cancer.

- Immunotherapy works better in patients with smaller tumor burden and is unlikely to work in patients who have had multiple lines of chemotherapy.

- The NCI Cancer Immunotherapy Trials Network is rapidly moving toward opening phase I immunotherapy trials and building collaborative efforts with multiple institutions that have various levels of expertise with different aspects of immunotherapy drug development. Other groups also are involved.

- Dr. Heery summarized four current immunotherapy platforms.
  1. In vivo inducers of tumor-specific immunity, commonly referred to as vaccines, are an effort to modify how the immune system recognizes cancer cells and teach the immune system to kill those cells. Vaccine therapies can be dendritic cells (e.g., PROVENGE), whole tumor cell vaccines (e.g., GVAX), vector-based vaccines (viral, yeast, etc.), DNA vaccines, or proteins (adjuvant vaccines).
  2. Adoptive transfer involves selection of activated T cells from the tumor site, growing them up to critical mass, and returning them to the patient (tumor infiltrating-lymphocytes, or TILs). A second adoptive transfer approach is to remove immune cells by apheresis, modify them to make them more active, grow them to critical mass, and return them to the patient (e.g., chimeric antigen receptors, T cell receptors). Adoptive transfer techniques can have significant toxicities.
  3. Checkpoint inhibition is based on the activity of anti-cytotoxic T-lymphocyte-associated antigen (CTLA-4), anti-programmed cell death protein 1 (PD-1), and anti-PD-L1. Ipilimumab (anti-CTLA-4) has been approved for treatment of metastatic melanoma. The anti-PD-1 and anti-PD-L1 agents are of great interest and demonstrate dramatic responses to melanoma, kidney cancer, and lung cancer.
  4. Immunostimulants and immunomodulators such as cytokines, antibody-cytokines conjugates, and indoleamine 2,3-dioxygenase (IDO) inhibitors are another approach but can have significant toxicity.

- Each platform has advantages and disadvantages. Some are expensive, but some are available off the shelf.

- Vaccines have minimal short-term benefit, and initial tumor shrinkage is rare. It is impossible to tell initially who will ultimately benefit. Progression-free survival is not a good measure of effect.

- Adoptive transfer can be unpredictable and is very expensive. It requires specialized manufacturing techniques for each patient and is difficult to administer in a community setting.

- Checkpoint inhibition can induce rapid reduction in large-volume disease with long-lasting benefit but is associated with significant adverse events, including death, although that is rare with the newer agents, anti-PD-1 and anti-PD-L1. Response in a variety of cancers indicates that this approach can be successful in treating any type of cancer.

- Combinations of immunotherapies and conventional treatments show promise.

- Targeting the PD-L1/PD-1 pathway can induce durable clinical responses in patients with a variety of tumor types.

- Heat shock protein inhibitors can cause tumor cells to upregulate certain antigens and make them more visible to the immune system. Work on this is preliminary.

- Advocacy groups can identify immune targets in their disease, assist investigators in getting grants, and help connect groups, as well as promote education around immunotherapy, playing an important role in recruiting patients for trials, and advocating for the FDA to allow novel trial designs.

- An actionable plan for the future involves designing early trials for the greatest likelihood of determining a clinical benefit and collecting as much data as possible for potential correlations, including looking for indicators of effect.

- The immune system also has a role in cancer prevention, but prevention trials can be challenging to design and conduct.

DCLG Working Group Updates

Organizational Engagement Working Group

- The group is in the beginning stages and looking for volunteers. Interested members can contact Mr. Retzlaff at jon.retzlaff@AACR.org.

Advocacy Engagement Working Group

- The group has developed a framework and completed a recommendation document and will move to the implementation stage. Nancy Roach, a member of the board of directors of Fight Colorectal Cancer, will serve as co-chair. Interested members can contact Ms. Harris at joya.harris@cancer.org.

Informed Consent Working Group

- The group is focused on developing an appropriate informed consent model to address the way cancer treatment is changing. The consent process must address the trend toward highly individualized treatment and the need to resample tumors over time. The group has formed a consortium with Johns Hopkins, Harvard/Dana-Farber, Harvard/Massachusetts General, and the Henry Ford Hospital systems and has begun processing samples of forms and collecting feedback from institutional review boards (IRBs). Volunteers are welcome and can contact Mr. Wallace at max.wallace@ABCC.org or at his cell phone, 919-368-2435.

Next Steps

- Ms. Bulman will explore ideas for developing immunotherapy as a topic for the October 2014 DCLG meeting and encourages members to reach out if they have specific thoughts on topic areas and speakers.