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JOURNAL OF CANCEROLOGY HOT TOPIC

Special Award Lecture Abstracts

David A. Karnofsky Memorial Award and Lecture

Saturday, May 30, 9:30 AM

PROGRAMMED DEATH-1 PATHWAY BLOCKADE: A COMMON DENOMINATOR FOR CANCER THERAPY

SUZANNE L. TOPALIAN

Johns Hopkins Kimmel Cancer Center, Baltimore, Maryland, USA

In the current era in oncology emphasizing personalized therapy, programmed death-1 pathway blockade is distinguished by its "common denominator" approach. The genetic diversity found in most human cancers creates challenges for therapies directed against individual mutations, but exposes a panoply of new targets for potential immune recognition. However, immune cells that recognize and are poised to attack cancer cells are held in check at the tumor site by suppressive molecular pathways (so-called immune checkpoints). Nearly 20 years ago, laboratory studies revealed that blocking the prototypical immune checkpoint cytotoxic T-lymphocyte antigen-4 could mediate tumor regression in murine models, leading to the clinical development and approval of anti-cytotoxic T-lymphocyte antigen-4 (ipilimumab) for treating patients with advanced melanoma in 2011. More recently, drugs blocking the distinct checkpoints programmed death-1 and its major binding partner programmed death-L1 have shown great promise in treating diverse cancer types. The realization that non-small cell lung cancer is susceptible to anti-programmed death-1/programmed death-L1 immediately broadened the horizon for cancer immunotherapy as a general treatment modality; lung and other common epithelial cancers had not previously responded to various immunotherapies and were thought to be relatively non-immunogenic.

Durable regressions of advanced treatment-refractory kidney, bladder, ovarian, and head and neck cancers, as well as melanoma and Hodgkin's lymphoma, following programmed death-1 pathway blockade have fueled the intensive examination of predictive biomarkers and a growing cohort of unique checkpoint molecules as potential drug targets.

These translational research efforts have provided new treatment options and are revolutionizing therapeutic algorithms. The complex biology of immune checkpoint pathways still contains many mysteries, and the full activity spectrum of drugs blocking these pathways, used alone or in combination, is unknown. Armed with new scientific understanding and unprecedented clinical opportunities, the field of immunotherapy is now standing on the threshold of even greater advances in the war against cancer.

Science of Oncology Award and Lecture

Sunday, May 31, 1:00 PM

IMMUNE CHECKPOINT BLOCKADE IN CANCER THERAPY: NEW INSIGHTS AND OPPORTUNITIES

James P. Allison

University of Texas MD Anderson Cancer Center, Houston, Texas, USA

The existence of multiple non-redundant I inhibitory pathways that limit T-cell responses offers novel strategies for mobilizing the immune system to attack cancer cells. The best characterized of these immune checkpoints is cytotoxic T-lymphocyte antigen-4, which inhibits CD28-mediated co-stimulation. Antibodies to cytotoxic T-lymphocyte antigen-4 have proven effective against multiple tumor types in both preclinical and clinical studies. Ipilimumab, an antibody to human cytotoxic T-lymphocyte antigen-4, showed long term (4.5 years) survival benefit in about 23% of patients in a randomized, placebo-controlled trial in late-stage melanoma. In 2011 the FDA approved it for treatment of late stage melanoma and it is now a standard of care for that disease.

The mechanism(s) of action of anti-cytotoxic T-lymphocyte antigen-4 are still being elucidated. Cytotoxic T-lymphocyte antigen-4 blockade results in an increase in the frequency of CD4 T-cell expression (inducible T-cell co-stimulator) in both tumor tissues and blood. This population contains a vast majority of tumor-specific cells that produce IFN and TNF. Using mouse models, we have shown that the inducible T-cell co-stimulator/inducible co-stimulator ligand pathway is critical for optimal antitumor activity of anti-cytotoxic T-lymphocyte antigen-4, and that inducible T-cell co-stimulator is a compelling molecule to develop as a target for agonistic targeting of co-stimulatory checkpoints. Programmed death-1, another checkpoint, works by interfering with T-cell antigen receptor signaling, a completely different mechanism from cytotoxic T-lymphocyte antigen-4. It has two ligands, programmed death-L1 and -L2, which are both expressed on dendritic cells. However, many tumor cells also express programmed death-L1.

Antibodies to programmed death-1 and -L1 have both shown objective responses against several tumor types in clinical trials, with response rates of about 25%. A recent phase II trial of a combination of anti-programmed death-1 and anti-cytotoxic T-lymphocyte antigen-4 in melanoma showed objective responses in about 50% of late-stage melanoma patients. Our studies of the mechanisms involved in the antitumor effects and of more effective combinations will be discussed.

2015 ASCO Annual Meeting Proceedings Special Awards 1s

ASCO–American Cancer Society Award and Lecture

Monday, June 1, 11:30 AM

CANCER PREVENTION AS OUR FIRST BEST HOPE: ACTION IN PREVENTION RESEARCH AND CANCER CONTROL

Ernest Hawk

Division of Cancer Prevention and Population Sciences, University of Texas MD; Anderson Cancer Center, Houston, Texas, USA

The global context of cancer is rapidly changing as the population ages and progressively adopts unhealthy lifestyles. It is anticipated that low-to-middle income countries will bear the majority of the future cancer burden. Cancer prevention will be critical to address this growing challenge. But in order to do so, concerted efforts are needed on two fronts: (i) discovery: to better understand at a molecular and cellular level what initiates and drives early cancer development to find effective screening tools and interventions that can be administered much earlier in the disease process; and (ii) dissemination: to use existing evidence to formulate and implement effective community oriented programs involving public policy, public education, and clinical preventive services that reduce cancer risks. National Cancer Institute-designated cancer centers are in a unique position to collaboratively advance prevention research and cancer control, and the Affordable Care Act is providing unprecedented opportunities to reimburse for clinical delivery of evidence-based preventive interventions. In both the clinical and population contexts, the ultimate goal is safe, timely, effective, efficient, equitable, patient-centered or culturally tailored preventive care, sustainable across time and populations. Together, the two complementary approaches of molecular prevention and cancer control offer an optimal approach to cancer – combining adoption and maintenance of healthy lifestyles, evidence-based screening, and early detection, with precision treatment of early stage lesions. Growing evidence supports the importance of such a strategy, demonstrating significant reductions in cancer risk as well as cardiovascular/cancer-related and all-cause mortality in those adhering to cancer prevention recommendations. To this end, we must aspire to elevate cancer prevention and control as the first strategy to address cancer, in every regard, everywhere, and by all means – whether through molecular prevention, lifestyle modifications, screening and early detection, or policy and educational initiatives.

B.J. Kennedy Award and Lecture for Scientific Excellence in Geriatric Oncology

Sunday, May 31, 9:45 AM

TRANSFORMING DATA INTO ACTIVITIES DESIGNED FOR OLDER CANCER PATIENTS

Silvio Monfardini

Istituto Palazzolo, Fondazione Don Gnocchi, Milan, Italy

Clinical oncologists should be well prepared for the inevitable increase of older cancer patients in the next decades.

Extensive data have been provided by many studies on the results of treatment for elderly patients in most tumor types and on the special approach needed to evaluate such patients. As a result, the International Society of Geriatric Oncology issued appropriate guidelines. Tools helping to predict treatment-related toxicity have been studied, and a specific methodology for clinical trials in

the elderly is now available. To acquire these data, the interaction between oncologists and geriatricians has been essential. In the United States, ASCO and NCI-NIA nationwide initiatives have been emphasizing dual training and research, whereas in France, a centralized universalistic approach aims at collaboration between geriatricians and oncologists. In some other European nations, several models of care delivery and cooperation have been developed. The integrated approach built up with these national initiatives needs to be reinforced and spread, providing the background for the implementation of new research projects. The main obstacles to taking action in the United States and Europe are the shortfall of geriatricians and their time constraint due to being engaged with other multiple tasks at their institutions, as well as the overwhelming numbers of older cancer patients. Local healthcare situations differ, but the best suited modality of cooperation among oncologists, geriatricians, and allied health professionals should always be found. Innovation through interaction with geriatricians should be brought into surgical oncology and even more in radiotherapy. A greater interaction is also necessary to study how to deliver optimal post-treatment care to older cancer survivors. Studies are also needed for frail cancer patients, the majority of whom are located in nursing homes.

Pediatric Oncology Award and Lecture Childhood cancer survivors: A lifetime of risk and responsibility

Saturday, May 30, 1:15 PM

AN AUTOBIOGRAPHY OF "WE"

Stephen E. Sallan

Dana-Farber Cancer Institute, Boston, Massachusetts, USA

Simultaneously stunning and yet unsurprising, over the past 40 years the collective endeavors of a relatively small community of pediatric investigators have fundamentally impacted the field of childhood cancer. Cure is expected for the vast majority of affected children. Today's research focuses on currently intractable variants of disease, more precisely targeted therapies, and diminution of the sequelae of curative treatments. With an emphasis on training and mentorship, and with recognition that every successful endeavor represents the intertwined and inseparable contributions of many individuals, this presentation will encompass the common ground and collective attributes of the pediatric oncology community. The community's commitment to discovery in the context of clinical trials and the importance of the two-way street between clinical investigators and basic science laboratories will be addressed. In essence, the presentation will consider the too-often overlooked "sociology" of our community: Who are we? How did we get here? How do we accomplish our work? Where are we going? An overview of our collective career journeys as one transitions from "I to We to Them."