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>
> Jedd Wolchok, MD, PhD, a lead investigator in the clinical trials

Ipilimumab uses a novel approach known as immunotherapy, which exploits the body's own immune system to attack cancer. The therapy, originally known as anti-CTLA-4, was developed in 1996 by James Allison, PhD, Chair of the Sloan Kettering Institute's Immunology Program at MSKCC. For more than 20 years, Dr. Allison's research has focused on the mechanisms that regulate the immunologic responses of T lymphocytes - commonly referred to as T cells - with an emphasis on manipulating T cell response in order to develop novel tumor immunotherapy approaches.

Over the years, Memorial Sloan Kettering researchers were deeply involved in preclinical and clinical studies using ipilimumab, most notably a 2009 phase II multicenter trial led by medical oncologist Jedd Wolchok, MD, PhD. Dr. Wolchok was a participant in the phase III trial, presented in 2010 at the American Society of Clinical Oncology annual meeting, which found a dose-response relationship to the drug in patients with stage III or IV disease. He also led a team in the development of a novel set of tumor-response criteria based on ipilimumab's unique mechanism of action.

Together, recent advances in understanding intracellular signaling pathways and immunotherapies such as ipilimumab to block those pathways have allowed clinicians to offer melanoma patients new treatment options for this disease.

“Ipilimumab is the first drug ever to be shown to produce an improvement in overall survival for patients with metastatic melanoma,” according to Dr. Wolchok. “This is a significant achievement in a disease which has been so resistant to standard therapies. It is also a great source of hope for patients as we now build on the success of ipilimumab with novel combination therapies.”

“The success of ipilimumab underscores the importance of basic research to clinical achievement,” Dr. Allison added. “The concept came directly out of our studies on fundamental mechanisms of regulation of T cell responses.”

In addition, researchers at the Center are studying biomarkers to help identify those patients who could benefit most from therapies like ipilimumab, and they have received a National Institutes of Health Grand Opportunity Stimulus award to study how the immune response to the NY-ESO-1 antigen is related to clinical outcome for ipilimumab therapy. This work, which is being conducted in several large clinical trials, is also supported by grants from Swim Across America, the Melanoma Research Alliance, and the Cancer Research Institute.

According to the National Cancer Institute, 68,130 new cases of melanoma were diagnosed in the United States in 2010, and 8,700 Americans died from the disease. Melanoma is the least common form of skin cancer, but is considered the most serious.