Promising treatment for metastatic melanoma 'fast tracked' by FDA

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Researchers from the John Theurer Cancer Center at Hackensack University Medical Center played an important role in a study that led to the Food & Drug Administration's (FDA) recent fast tracking of ipilimumab, a promising treatment for metastatic melanoma. The FDA based its decision largely on the results of a pivotal study published in the *New England Journal of Medicine* on August 19, 2010 - the same day the agency accepted Bristol-Myers Squibb's application for the drug's approval and granted the application priority review status.

Ipilimumab is the first drug shown in randomized, placebo-controlled trials to improve survival in stage IV melanoma.

"This study, and the FDA's decision, provides new hope for people with this devastating cancer," said Andrew L. Pecora, M.D., F.A.C.P., C.P.E., Chairman and Executive Administrative Director, John Theurer Cancer Center, who led the study at the John Theurer Cancer Center. "We are proud to have played a role in helping move another promising cancer treatment closer to market."

The incidence of metastatic melanoma has increased over the last three decades, and the death rate continues to climb faster than that of most other cancers. According to the American Cancer Society, there were approximately 68,000 new cases of melanoma in the United States in 2009, and 8,700 melanoma-related deaths. Melanoma accounts for about three percent of all skin cancers, but 80 percent of skin cancer deaths. Melanoma is difficult to treat once it has spread beyond the skin to other

parts of the body (metastasized). Very few treatment options exist for people with metastatic melanoma.

In this phase III study, researchers randomly assigned patients to one of three treatment groups: those receiving ipilimumab plus an inactive (placebo) version of gp 100, a cancer vaccine; those receiving ipilimumab plus gp 100; and those receiving gp 100 plus ipilimumab placebo. The treatments were administered once every three weeks, for a total of four treatments. The study was double blinded: neither the researchers nor the patients knew which medications the patients were being given.

To participate in the study, patients must have had stage III or IV (metastatic) melanoma, and must have been previously treated unsuccessfully with another cancer drug. They must also have had a life expectancy of at least four months. 676 patients participated in the study at 125 cancer centers.

Those who received ipilimumab, both by itself and with gp 100, lived a median of about 10 months, while those who received only gp 100 lived about 6.4 months. After two years, approximately 23 percent of those who got ipilimumab were alive, while 14 percent of those who did not receive this drug survived. Ten to 15 percent of those who received ipilimumab suffered attacks on their bodies' immune systems (autoimmune reactions), and seven of the 540 patients who got this drug died from these attacks. Most adverse events suffered by study participants, however, were reversible with treatment.

A monoclonal antibody, ipilimumab activates the body's immune system to fight cancer by blocking a protein called CTLA-4. CTLA-4 is a molecule on T-cells, white blood cells that play a critical role in regulating immune responses. CTLA-4 suppresses the immune system's response to disease, so blocking its activity stimulates the immune

system to fight the melanoma.

The FDA grants priority review status to drugs that offer major advances in treatment, or that provide treatment where no adequate therapy exists. The projected FDA action date for the ipilimumab application is December 25, 2010.

The John Theurer Cancer Center has more than 100 clinical trials under way for all types of cancer and life-threatening blood disorders. Clinical trials test the safety and effectiveness of new medications, therapies, treatment regimens, devices, and adjuvant treatments in human patients. These clinical trials are conducted independently or in cooperation with pharmaceutical companies, universities, other cancer centers, and national organizations such as the National Cancer Institute, the American Cancer Society, the National Science Foundation, and the National Institutes of Health.

"Our commitment to providing outstanding patient care and leading edge treatments extends to our leadership or participation in major clinical trials," said Dr. Pecora. "We are dedicated to improving treatment outcomes not just for our patients, but for all of those with cancer."

Provided by John Theurer Cancer Center