Promising drug prevents cancer cells from shutting down immune system

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(Medical Xpress)—An investigational drug that targets the immune system's ability to fight cancer is showing promising results in Yale Cancer Center (YCC) patients with a variety of advanced or metastatic forms of the disease. Updated data from this Phase 1 clinical trial are being formally presented at the 2013 annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago. Yale Cancer Center is one of the lead trial sites. The abstract was made public by ASCO in advance of the meeting.

The drug, known as MPDL3280A and manufactured by Roche Genentech, is designed to prevent a cancer cell's mutated and overexpressed PD-L1 gene protein from putting the immune system to sleep. The overexpressed PD-L1 protein turns off the immune system's T-cells by binding to its PD-1 and B7.1 proteins. In doing so, it disguises itself and evades detection and destruction by the body's immune response.

This new drug is the latest advance in the burgeoning field of immunotherapy, which aims to boost the body's immune system to fight the foreign pathogens of cancer. By blocking the cancer tumor's PD-L1 protein, MPDL3280A frees the immune system to do its job. This PD-L1 targeted antibody was specially engineered to increase safety and efficacy over earlier immunotherapy agents.

Yale oncologists report that the efficacy of MPDL3280A was evaluated in 140 patients with locally advanced or metastatic solid tumors who had exhausted other means of therapy. Tumor shrinkage was observed in patients with non-small cell lung cancer, melanoma, kidney cancer, colorectal cancer, and gastric cancer. Yale oncologists say ongoing, durable responses were observed in nearly all patients who responded to the drug. Overall, 29 out of 140 patients (21 percent) experienced significant tumor shrinkage, and the highest number of responses were in patients with lung cancer and melanoma.

MPDL3280A was generally well tolerated, they say, with few immune-related adverse events. Some patients were continuing to respond more than a year after starting treatment.

"We have been very impressed by the response in seriously ill patients whose cancer had metastasized. So far, almost none of those who showed tumor shrinkage have gotten worse, which is extraordinary," said lead author Roy Herbst, M.D., professor of medicine and chief of

medical oncology at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. "Immunotherapy treatment is providing new hope for cancer patients," he added.

Further studies will be needed, including randomized clinical trials, to confirm the safety and effectiveness of MPDL3280A, and to develop methods to determine whether a patient will indeed respond to the anti-PD-L1 drug.

Provided by Yale University