Engineered antibody demonstrated safety, efficacy in wide range of advanced tumors

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(Medical Xpress)—The engineered antibody MPDL3280A, which targets a protein called programmed death-ligand 1 (PD-L1), was safe and effective for several cancers, according to phase I study results presented at the AACR Annual Meeting 2013, held in Washington, D.C., April 6-10.

"Our PD-L1 antibody was well tolerated, and there were no limiting toxicities," said Michael S. Gordon, M.D., research director at Pinnacle Oncology Hematology in Scottsdale, Ariz. "It was active with antitumor activity across a broad range of cancers, and we have developed biomarker tools that we are testing, which may allow us to optimize patient selection for this novel therapy."

PD-L1, a protein found on the surface of many cancer cells, impairs the immune system's ability to fight cancer, according to Gordon.

"PD-L1 is essentially a plug, which inserts into an outlet (PD-1) on the surface of the immune T cells," Gordon said. "As the T cells come close to the tumor, for example, they are engaged by PD-L1, which inserts into the outlet on the surface of the T cell. That starts a signal inside the T cell that blocks the T cell's ability to kill the cancer cell."

MPDL3280A, a human monoclonal antibody under development by Genentech, a member of the Roche Group, binds to PD-L1 and blocks this action.

Gordon and colleagues administered an escalating intravenous dose of MPDL3280A once every three weeks to 30 patients with a variety of locally advanced or metastatic solid tumors. They escalated the dose from 0.01 mg/kg to as high as 20 mg/kg. The data being presented are the preliminary data from the dose escalation cohorts of the ongoing phase I trial.

No dose-limiting toxicities or grade 4 adverse events have been reported. "We were able to escalate to the top dose without being limited by any serious side effects," Gordon said.

"From a therapeutic standpoint, we were able to identify a number of patients with a broad range of diseases, including lung cancer, kidney cancer, colon cancer and stomach cancer, who responded to the treatment," he said.

A second protein, called PD-L2, fits into the same T-cell "outlet" as PD-L1, according to Gordon. MPDL3280A is specific for PD-L1; it does not block PD-L2, which is expressed in noncancerous tissues including the lung, he added.

"One would anticipate, compared with drugs being developed to specifically block the T-cell outlet (PD-1) and, therefore, block the relationship between the outlet and both PD-L1 and PD-L2, that we might see less lung or pulmonary toxicity with MPDL3280A. But we need to conduct larger studies to confirm this."

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