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New Drug May Help Immune System Fight Cancer

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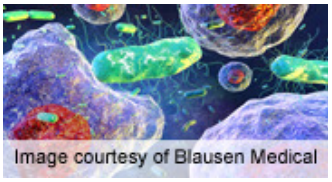
Image courtesy of Blausen Medical

THURSDAY, May 16 (HealthDay News) -- An experimental drug that taps the power of the body's immune system to fight cancer is shrinking tumors in patients for whom other treatments have failed, an early study shows.

The drug binds to a protein called PD-L1 that sits on the surface of cancer cells and makes them invisible to the immune system, almost like a cloaking device.

"That [the protein] allows the tumor cell to grow unchecked and cause harm to the patient," said study author Dr. Roy Herbst, chief of medical oncology at Yale University.

But with the protein blocked, the immune system can see and destroy cancer cells.

Of 140 patients in the pilot safety study, 29 (or 21 percent) initially saw significant tumor shrinkage after at least three months on the medication. Researchers say 26 patients have continued to respond over time, including some who have been on the drug for more than a year. One patient saw tumors disappear completely.

The drug also seems to work on a wide range of cancers, including some of the toughest to treat, including non-small cell lung cancer, melanoma skin cancer, colorectal cancer, kidney cancer and stomach cancer.

"This has all the characteristics of a really amazing drug," said Herbst, who has been testing new cancer medications for two decades. "I can count on one hand the number of times I've seen response rates like this."

The study was funded by Genentech/Roche, the company that is developing the drug. The results were presented at a Wednesday news conference organized by the American Society of Clinical Oncology in advance of its annual meeting, which starts May 31 in Chicago.

Study results presented at medical meetings are considered preliminary because they have not been subjected to the rigorous scrutiny required for publication in a medical journal.

At least four other companies -- Merck, Bristol-Meyers Squibb, MedImmune and Amplimmune -- also are racing to develop drugs that target PD-L1 or the molecule that binds to it (PD-1).

"I don't think in the history of cancer therapy have you had five or more companies virtually simultaneously developing antibodies targeted at the same pathway," said Dr. Drew Pardoll, co-director of cancer immunology at the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, in Baltimore.

Pardoll is testing a drug that targets PD-1 for Bristol-Myers Squibb. He was not involved in the current study.

The drugs are part of a wave of new treatments that work by spurring the immune system to take on tumors. These drugs are building on the successes of medications like Provenge, the first cancer immunotherapy, which was approved in 2010 to treat prostate tumors, and Yervoy, which was approved in 2011 to treat metastatic melanoma.

Yervoy works early in the immune reaction to wake up T-cells that are essentially napping on the job, Pardoll said. The PD-1 and PD-L1 drugs work later, at the cellular level.

"This is a whole new kind of treatment, and the early data has looked so impressive," Pardoll said. "I think this just reflects the excitement among biotechnology companies and big pharma in this field."

To understand why researchers are excited, it helps to understand how poorly most cancer drugs perform in early trials. A study published in the journal *Clinical Cancer Research* in August 2005 found that middle-of-the-road response rates for cancer drugs in early trials was just 3 percent, with the best response rate topping out at 18 percent.

Response rates are so dismal in part because doctors usually don't try unproven drugs in cancer patients until they have run out of other options. All the patients in this study had seen their cancer progress despite several prior treatments. Most had seen their cancer spread beyond its original site.

Pardoll said he also has been impressed with the length of time that patients continue to see benefits from the medications in the new study.

"Among the patients that did respond to anti-PD-1, who had been followed for more than a year, roughly two-thirds were still in a response a year out," he said. "That's something you don't see with chemotherapy; you don't see it with current targeted therapies.

"We think this is because the immune system is being re-educated," Pardoll said. "If that's the case, will we be able to discontinue the antibody and have the patient's immune system take over and keep the cancer at bay?"

Although the drugs have great promise, the researchers said they also were keeping an eye on the adverse events they can cause, some of which have been very serious.

PD stands for programmed death, and together the two molecules work to switch off the body's immune response. Blocking one or the other keeps the immune system active, which is good for fighting cancer, but there are also early signs that manipulating this response may have a downside.

Some patients had side effects that researchers believe are caused by autoimmunity -- the body mistakenly attacking its own organs and tissues. Those side effects include lung and liver inflammation, rashes and hypoglycemia (low blood sugar), perhaps because of a problem with the thyroid gland.

In a study published in a June 2012 issue of the *New England Journal of Medicine*, three patients who were taking an anti-PD-1 drug died from pneumonitis, or inflammation of the lungs.

The researchers said they're working to understand why the drugs seem to be particularly toxic to the lungs and to mitigate their adverse effects.

"We need to be cautious about the toxicities," Herbst said. "It's great that we're making progress, and now we need to go to randomized trials."

More information

To find clinical trials that are testing immunotherapy drugs, head to the Cancer Immunotherapy Trials Network.

SOURCES: Roy Herbst, M.D., Ph.D., chief, medical oncology, Yale University, New Haven, Conn.; Drew

Ph.D., co-director, cancer immunology, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore; May 15, 2013, press briefing, American Society of Clinical Oncology

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