New antibody drug engages the immune system in fight against cancer

Yale UniversityYale University

About a quarter of patients with deadly cancers had significant reductions of tumor size after taking a new antibody drug, according to results of a large early-stage clinical trial conducted by scientists from Yale School of Medicine, Johns Hopkins University, Harvard University, Bristol-Myers Squibb, and other major institutions. The study appears in the New England Journal of Medicine. The findings are also being presented at the annual meeting of the American Society of Clinical Oncology.

Nearly 300 patients with advanced melanoma, non-small cell lung cancer, or renal cell cancer whose cancer progressed after receiving standard treatments were given the drug, which boosts the immune system's capacity to fight cancer.

"This is the first agent that blocks the tumor's ability to fend off the cancer-fighting cells of the immune system," said senior author Mario Sznol, M.D., professor of medicine at Yale School of Medicine and co-director of the melanoma program at Yale Cancer Center [1].

The study drug — BMS-936558 (MDX-1106, anti-PD-1), manufactured by Bristol-Myers Squibb — is an antibody designed to block a protein known as "programmed death-1" (PD-1), which is present on the surface of immune lymphocyte cells (types of white blood cells) and inhibits their function. Administration of BMS-936558 is thought to restore the function of cancer-fighting lymphocytes.

Anti-PD-1 was administered to 296 patients whose cancer had grown despite standard treatment. Tumor shrinkage of at least 30 percent was seen in 18 percent of the lung cancer patients, 28 percent of the melanoma patients, and 27 percent of the renal-cell patients. Overall, anti-PD1 was generally well tolerated by patients, although a few patients developed severe and sometimes life-threatening side effects. Researchers reported that patients' response to the drug tended to be long-lasting, in some cases more than a year.

Researchers were particularly intrigued by the response of patients with lung cancer, a type of cancer that many researchers thought would not be responsive to immune therapies.

"I believe we can extend these treatments to other types of cancer, and have great hope to improve them further by combining with other kinds of anti-cancer drugs," Sznol said.

Co-author Lieping Chen, M.D., professor of immunobiology, medicine, and dermatology at Yale School of Medicine and director of the cancer immunology program at Yale Cancer Center, has made major contributions to the discoveries of

these immune molecules, including the suppressive mechanisms of PD-1 and its two ligands, PD-L1 and PD-L2.

“We are now all convinced that our own immune system is very powerful if it is switched on in the right way. It is also particularly exciting and rewarding to see the discoveries made in the laboratory being translated into clinical trials,” Chen said.

Co-author Scott Gettinger, M.D., associate professor of medicine at Yale School of Medicine, who treated the most patients with lung cancer taking part in the multi-center trial, is working with Chen and other scientists at Yale to understand why some patients respond and others didn’t respond to anti-PD1 treatment.

“We have seen promising results in this study, with some dramatic responses in patients that appear to be long lasting in most cases,” Gettinger said. “Furthermore, this therapy has been well tolerated, markedly better than other available salvage therapies that are associated with low response rates.”

Other authors are; Suzanne L. Topalian (first author), Julie R. Brahmer, Charles G. Drake, Drew M. Pardoll, William H. Sharfman, Robert A. Anders, Janis M. Taube, Tracee L. McMiller, and Haiying Xu of Johns Hopkins University and the Sidney Kimmel Comprehensive Cancer Center; F. Stephen Hodi of the Dana-Farber Cancer Institute; David C. Smith of the University of Michigan; David F. McDermott and Michael B. Atkins of Beth Israel Deaconess Medical Center; John D. Powderly of the Carolina BioOncology Institutes; Richard D. Carvajal of Memorial Sloan-Kettering Cancer Center; Jeffrey A. Sosman and Leora Horn of Vanderbilt University Medical Center; Philip D. Leming of Cincinnati Hematology-Oncology, Inc.; David R. Spigel of the Sarah Cannon Research Institute/Tennessee Oncology; Scott J. Antonia of the H. Lee Moffitt Cancer Center and Research Institute; and Alan J. Korman, Maria Jure-Kunkel, Shruti Agrawal, Daniel McDonald, Georgia D. Kollia, Ashok Gupta, and Jon M. Wiggington of Bristol-Myers Squibb.

The study and clinical trial were funded by Bristol-Myers Squibb, Ono Pharmaceuticals, and grants from the National Institutes of Health and the Melanoma Research Alliance.

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