

## New immune therapy shows promise in kidney cancer

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An antibody that helps a person's own immune system battle cancer cells shows increasing promise in reducing tumors in patients with advanced kidney cancer, according to researchers at Beth Israel Deaconess Medical Center.

The results of an expanded Phase 1 trial presented at the American Society of Clinical Oncology's annual conference in Chicago, showed that some patients treated with a fully <u>human monoclonal antibody</u> developed by <u>Bristol Myers Squibb</u> had a positive response to the effort by the agent, BMS-936558, to prolong the immune system's efforts to fight off <u>renal cell carcinoma</u> without some of the debilitating side effects common to earlier immunotherapies.

The presentation by David F. McDermott, MD, Director of Biologic Therapy Program at the Beth Israel Deaconess Medical Center Cancer Center and an Assistant Professor of Medicine at Harvard Medical School, highlights one of two key efforts underway to use the body's own disease-fighting tools against cancer.

Separate work by David Avigan MD, Director of BIDMC's Blood/<u>Bone</u> <u>Marrow Transplant</u> Program, focuses on developing a personalized vaccine, compromised of the patient's tumor and <u>immune system</u> agents, to battle <u>kidney cancer</u>.

<u>Cancer cells</u> have the ability to trick the immune system, the body's selfdefense mechanism, which is designed to ward off infections. Immune



therapy such as <u>antibody treatment</u> and vaccines is designed to reeducate the body to recognized cancer as an invader.

"We've known for a long time that in certain cases the immune system can be boosted in a way that can create remissions" of <u>hematologic</u> <u>malignancies</u> like leukemia and lymphoma, says McDermott. "We've been trying to create the same long term results in solid tumors, which is more difficult."

In this trial, the antibody was designed to block the Programmed Death (PD)-1 inhibitory receptor expressed by activated T cells. PD-1 acts a natural shut off valve for T cells. By blocking its action, these cells can be revived to fight cancer. In the initial portion of the trial, the agent showed "promising" activity in patients with various solid tumors, including metastatic renal cell carcinoma, melanoma and lung cancer.

In an expanded trial, patients received up 10 mg/kg of an intravenous treatment twice weekly, followed by 1 mg/kg. Patients received up to 12 cycles of treatment until either progressive disease, unacceptable toxicity or a complete response was detected.

"These antibodies were developed based on an understanding of how the immune system is not well designed to fight cancer," says McDermott. "Your immune system is in place to help fight off infections. So when you have a viral infection, it will turn on in response to that infection and once it's controlled will shut down. The shut off valves, like PD-1, are actually stronger the pathways that turn on the immune system and this makes cancer difficult to control. The new PD-1 blocking antibody prevents this natural shutoff and allows T-cells to recognize and kill tumors."

McDermott noted that unlike current immunotherapies using interleukin-2, patients do not need to be hospitalized and suffer far less



significant side effects such as skin rash or nausea.

"We realized that we could this drug at the highest doses without developing many significant or too dangerous side effects," says McDermott. "Once we realized the drug was relatively safe to give, we expanded into larger numbers of patients who seem to be benefiting early on from this treatment."

McDermott cautions that it is too early in a Phase I trial, designed principally to test side effects and the best dosage and schedule of treatment, to draw sweeping conclusions from the results.

"We have seen about 30 percent of the patients with kidney cancer have major responses to this line of treatment. A similar 30 percent of melanoma patients have had major response to treatment and there are much more melanoma patients in this study than kidney cancer patients. And maybe 20 percent or so of <u>patients</u> with lung cancer have had major benefit."

## Provided by Beth Israel Deaconess Medical Center

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