Researchers find success with new immune approach to fighting some cancers

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A national research collaboration of senior researchers, including a researcher from Moffitt Cancer Center, has found that 20 to 25 percent of "heavily pre-treated" patients with a variety of cancers who enrolled in a clinical trial had "objective and durable" responses to a treatment with BMS-936558, an antibody that specifically blocks programmed cell death 1 (PD-1). PD-1 is a key immune "checkpoint" receptor expressed by activated immune cells (T-cells) and is involved in the suppression of immunity.

The clinical trial, designed to assess the anti-tumor activity and safety of the treatment, was conducted with the help of 296 patients with a variety of cancers, including non-small cell lung cancer, melanoma and renal cell cancer, among others. Study results were published in a recent article in The New England Journal of Medicine.

According to study co-author Scott J. Antonia, M.D., Ph.D., chair of the Thoracic Oncology Program and co-chair of the Immunology Program at Moffitt, tumors can develop multiple resistance mechanisms to evade natural destruction by the body's immune system. Tumors may do this by exploiting a variety of biochemical pathways that lead to "immune checkpoints" where immune responses that might get through the checkpoints and otherwise help destroy tumor cells are, instead, terminated.

"There have been recent intensive efforts to develop immunotherapeutic approaches to treat cancer, including efforts to develop immune-

checkpoint-pathway inhibitors," Antonia said. "A particular challenge in cancer immunotherapy has been to find the mechanism-based biomarkers that could be used to identify patients whose tumors are candidates for immune treatment."

For evidence that this approach is working, the study authors pointed to the recent success of the drug ipilimumab, an immune checkpoint pathway inhibitor that has been effective for many patients with advanced melanoma.

Their study results, Antonia said, suggested that tumors expressing the PD-1 ligand - PD-L1 (a ligand is binding molecule) - is an important candidate molecular marker. For example, in patients with PD-L1-positive tumors, the response to BMS-936558 was 36 percent, as opposed to no response in patients with PD-L1-negative tumors.

Among the 296 patient volunteers in whom responses could be evaluated, complete or partial responses resulted for those with non-small cell lung cancer, melanoma or renal cell cancer. The researchers concluded that the anti-PD-1 antibody was safe, effective and the responses were "durable."

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