Investigational drug may increase survival for some patients with advanced melanoma

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An experimental drug aimed at restoring the immune system's ability to spot and attack cancer halted cancer progression or shrank tumors in patients with advanced melanoma, according to a multisite, early-phase clinical trial at Johns Hopkins Kimmel Cancer Center and 11 other institutions. All patients had experienced disease progression despite prior systemic therapies, and most had received two or more prior treatments.

Patients who showed responses to the drug, nivolumab (anti-PD-1; BMS-936558; MDX-1106; ONO-4538), survived for an average 16.8 months following initiation of treatment. Overall, 62 percent of patients (66 of 107) were alive one year following treatment initiation, and 43 percent (46 of 107) were alive two years later. Average survival among 33 patients (31 percent) whose tumors shrank significantly was two years. The drug is now being tested in three larger, phase III trials in melanoma, which generally compare a new therapy with a standard one currently in use.

Results of the study are published online March 3 in the *Journal of Clinical Oncology*.

"The results seen here are remarkable for these patients with treatment-resistant, advanced metastatic melanoma, who had limited life expectancies when they joined the trial," says study lead-author Suzanne Topalian, M.D., professor of surgery and oncology, and director of the melanoma program at Johns Hopkins.

The immune-based therapy aims not to kill cancer cells directly, but to block a pathway that shields tumor cells from immune system components that are potentially able and poised to fight cancer. The pathway includes two proteins called programmed death-1 (PD-1), expressed on the surface of immune cells, and programmed death ligand-1 (PD-L1), expressed on cancer cells. When PD-1 and PD-L1 join together, they form a biochemical shield protecting tumor cells from being destroyed by the immune system. Another protein involved in the pathway, that is expressed by some tumors and by cells in the immune system, is programmed death ligand

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