

Biomarker identifies melanoma patients who may respond to immunotherapy MK-3475

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Among melanoma patients treated with the PD-1 inhibitor MK-3475, those whose tumors had the protein PD-L1 had better immune responses and higher survival rates, according to results presented here at the AACR Annual Meeting 2014, April 5-9.

When the protein PD-L1, which is present on some melanoma tumors, binds to PD-1, a protein present on T cells, "brakes" are applied on these T cells, preventing them from attacking the cancer cells. The immunotherapy MK-3475 blocks PD-1, releasing the brakes on T cells and enabling them to attack the [cancer cells](#).

This study found that among melanoma patients who received MK-3475, those whose tumors had PD-L1 had an overall response rate of 46 percent, while those whose tumors did not have PD-L1 had an overall response rate of 17 percent. At six months, 64 percent of the patients whose tumors were PD-L1-positive had no disease progression, compared with 34 percent of those whose tumors were PD-L1-negative. Similarly, 86 percent of the patients whose tumors were PD-L1-positive were alive after one year, compared with 72 percent of those whose tumors were PD-L1-negative.

"We found a major difference in the response rates between patients with PD-L1-positive and PD-L1-negative tumors treated with MK-3475," said Adil I. Daud, M.D., co-director of the UCSF Melanoma Center, and director of melanoma clinical research at the UCSF Helen Diller Family Comprehensive Cancer Center. "This is the largest data set

yet, to my knowledge, looking at PD-L1 expression in tumors from melanoma patients treated with PD-1 inhibitors.

"Data from this study identifies PD-L1 as a robust marker in determining which melanoma patients may be well served when treated with MK-3475. However, we are studying more samples from randomized trials of PD-1 inhibitor versus ipilimumab or chemotherapy to establish the validity of this marker," added Daud.

To evaluate the relationship between [tumor](#) PD-L1 expression and clinical outcome, Daud and colleagues studied tumor samples collected from 195 patients recruited to a phase I clinical trial testing MK-3475 at three different doses. All patients had late-stage [melanoma](#), and some of them had received prior treatment with another immunotherapy drug called ipilimumab.

The investigators measured the amounts of PD-L1 in the tumor samples and considered them PD-L1-positive if at least one cell per 100 tumor cells had the protein. They found that, of the 125 evaluable tumor samples, 89 were PD-L1-positive and 36 were PD-L1-negative.

Patients with PD-L1-positive tumors had disease that did not progress for about 50 weeks, while disease progressed at about 12 weeks for those with PD-L1-negative tumors.

The investigators also found that among patients whose tumors were PD-L1-positive, overall response rates between those who had and had not received prior therapy with ipilimumab (44 percent versus 47 percent) were not significantly different. Similarly, among patients whose tumors were PD-L1-negative, overall response rates between those who had and had not received prior therapy with ipilimumab (14 percent versus 17 percent) were not significantly different.

"This suggests that prior treatment with the anti-CTLA-4 antibody ipilimumab does not impact the ability of these tumors to respond to MK-3475, nor does it affect the viability of PD-L1 as a marker of response to MK-3475," said Daud.

The investigators found a 24 percent and 17.5 percent increase in two types of activated T cells, CD8-positive and CD4-positive T cells, in the blood of patients treated at three different doses of MK-3475 for six weeks, leading them to suggest that the treatment improved the immune response in these [patients](#) at all doses tested.

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