Trials show immune drugs effective in advanced melanomas

June 1 2015, by Garth Sundem

Rene Gonzalez, M.D. Credit: University of Colorado Cancer Center

Results of two clinical trials reported at the American Society for Clinical Oncology (ASCO) Annual Meeting 2015 show continued promise of immune therapies nivolumab and pembrolizumab against advanced melanomas, specifically in the context of PD1 signaling that some tumors use to avoid immune system attack. Dr. Rene Gonzalez, MD, investigator at the University of Colorado Cancer Center and director of the Melanoma Research Clinics at the CU School of Health, is an author of both studies.

In the phase III trial CheckMate 067, the combination of nivolumab with ipilimumab shows, "better efficacy but more toxicity," Gonzalez says,

suggesting that the combination might be most appropriate for patients whose melanomas do not over-express the protein PDL1, which can be targeted by other drugs. "Maybe PDL1-negative patients will benefit most from the combination, whereas PDL1-positive patients could use a drug targeting that protein with equal efficacy and less toxicity," Gonzalez says. Full results were presented in a plenary session this morning.

Results of the KEYNOTE-002 clinical trial show that not only does the immune therapy drug pembrolizumab improve survival of patients with metastatic melanoma over the use of chemotherapy alone, but that its benefit is not limited to patients whose cancers over-express the PDL1 protein.

In the current trial, of 179 patients who received chemotherapy alone, the disease of 16 percent remained controlled at 6 months. Of 361 patients who received pembrolizumab, 36 percent remained progression-free at 6 months (more than double the percentage of chemotherapy alone). The median duration of response for patients on chemotherapy alone was 37 weeks; the duration of the response in patients who took pembrolizumab was not reached during the time of the study.

There are two major players in the ability of melanomas to evade the body's immune system, the "don't attack" protein PDL1 on the tumors and the corresponding PD1 receptors on the immune system's T-cells. Pembrolizumab works by blocking these T-cel PD1 receptors, thereby disallowing interaction between PDL1 and PD1 and leaving the immune system primed to attack tumor tissue.

Pembrolizumab was approved in 2014 under the FDA Fast Track Development Program for the treatment of metastatic melanoma that had progressed after treatment with the first-line immune therapy drug ipilimumab and, if BRAF mutant, also a BRAF inhibitor.

"In metastatic melanoma, all patients and not just those who are PD-L-1 positive may benefit from pembro," says Rene Gonzalez,

Provided by University of Colorado Denver