

Adding the IDO-pathway inhibitor indoximod to pembrolizumab improved the melanoma response rate

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Adding the investigational immunotherapy indoximod to the FDA-approved immunotherapy pembrolizumab (Keytruda) increased the proportion of patients with advanced melanoma who responded to treatment compared with previously reported response rates for pembrolizumab monotherapy, according to interim results from a phase I/II clinical trial presented here at the AACR Annual Meeting 2017, April 1-5.

"In the phase III KEYNOTE-006 clinical trial that led the FDA to approve the [immune checkpoint inhibitor](#) pembrolizumab as an initial treatment for patients with advanced melanoma, the overall response rate was 33 percent, meaning 33 percent of patients had partial or complete shrinkage of their tumors," said Yousef N. Zakharia, MD, assistant professor in the Department of Internal Medicine at the University of Iowa, Iowa City. "We set out to investigate whether we could improve upon this response rate by adding an inhibitor of the IDO pathway to pembrolizumab treatment.

"We are excited to share interim results from the phase II portion of this clinical trial, because the data show that 52 percent of patients treated with a combination of pembrolizumab and the IDO-pathway inhibitor indoximod had a partial or complete response without significant added toxicities," continued Zakharia, who is also coleader of the early phase [clinical trials](#) program at the Holden Comprehensive Cancer Center at

the University of Iowa.

"It is noteworthy that this trial did not exclude ocular melanoma, which has been shown to be more aggressive and less responsive to available systemic treatment," added Zakharia. "Most comparable [trials](#) do not allow patients with ocular melanoma. When the results are considered without the [ocular melanoma](#) patients (9 out of 60), the response rate in cutaneous and nonocular melanoma is actually 59 percent. These robust data are very promising, but we need to confirm the clinical benefit in a larger, randomized trial."

Zakharia explained that the normal function of the IDO pathway is to keep the immune system in check, preventing it from responding inappropriately; for example, it helps prevent the immune system of a pregnant woman from attacking her baby. "However, some tumors hijack the pathway, using it to prevent the immune system from attacking and destroying the tumors, suggesting that it could be a good target for cancer immunotherapy," he said.

Previously reported results from the phase Ib portion of the clinical trial showed that the combination of indoximod and an FDA-approved immune checkpoint inhibitor called ipilimumab (Yervoy) was well tolerated and caused no increase in toxicity compared with the immune checkpoint inhibitor used alone.

In the phase II portion of the clinical trial, patients received indoximod and FDA-approved immune checkpoint inhibitor therapy of the treating physician's choice, either ipilimumab, pembrolizumab, or nivolumab (Opdivo). Most patients received indoximod (1200 mg orally twice every day) with [pembrolizumab](#), which was infused at the standard dose of 3 mg/kg every 21 days.

The new data being reported were obtained with a January 2017 cutoff

data. After a median follow up of 10.5 months, six of 60 patients had a complete response and 25 had a partial response, giving an overall response rate of 52 percent. The most common adverse events were fatigue, diarrhea, and nausea.

"The trial is still accruing patients and we are continuing to monitor all of the patients enrolled so far," said Zakharia. "This interim analysis represents the largest reported number of [melanoma patients](#) treated with the combination of an IDO-pathway inhibitor and standard checkpoint inhibitors to date."

According to Zakharia, the main limitation of the study is that the clinical trial had no control arm, which means that a large-scale, placebo-controlled randomized clinical is needed to confirm the current results.

Provided by American Association for Cancer Research

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