New immunotherapy combination shows promise for patients with advanced melanoma

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Treatment with a combination of ipilimumab (Yervoy) and Coxsackievirus A21 (CVA21; Cavatak) led to durable responses in a number of patients with advanced melanoma, including some whose melanoma had progressed despite prior treatment with an immune checkpoint inhibitor, and fewer than anticipated adverse events, according to results from a phase Ib clinical trial presented here at the AACR Annual Meeting 2017, April 1-5.

"In recent years, the number of treatment options for patients with advanced melanoma has increased with the development of immune checkpoint inhibitors such as ipilimumab," said Brendan D. Curti, MD, director of the Clinical Biotherapy Program and codirector of the Melanoma Program at the Earle A. Chiles Research Institute of Providence Cancer Center in Portland, Oregon. "However, not all patients respond to these immunotherapeutics and some who respond go on to have disease progression later. These patients have few treatment options and a poor outlook.

"We are excited that the ipilimumab–CVA21 combination has yielded responses greater than six months for a number of patients, both those whose melanoma has progressed after immune checkpoint inhibitor therapy and those who have not yet been treated with these immunotherapeutics," continued Curti. "Based on these promising preliminary data and the urgent need for new treatments for advanced melanoma patients refractory to immune checkpoint inhibitors, we are expanding the trial up to 70 patients."

CVA21 is bioselected, nongenetically altered common cold RNA virus. According to Curti, it can directly infect many different cancer cells and as such it can boost adaptive and innate anticancer immune responses.

Curti and colleagues are enrolling up to 70 patients with advanced melanoma in the melanoma intratumoral Cavatak and ipilimumab (MITCI) clinical trial. Patients who have and who have not received immune checkpoint inhibitors are eligible for the trial. CVA21 is injected directly into melanoma lesions, while ipilimumab is infused intravenously.

At data cutoff for this presentation, 25 patients were evaluable for safety and 22 were evaluable for response. The overall response rate was 50 percent, with four patients having a complete response and seven patients having a partial response. The median duration of response has not been reached, with a number of responses greater than six months and several still ongoing.

Among the 11 patients who had disease progression despite prior treatment with an immune checkpoint inhibitor, four had a response. The other seven patients who had a response had not previously received treatment with an immune checkpoint inhibitor.

"The preliminary overall response rate of 50 percent is very positive because previous reports indicate an 11 percent overall response rate for ipilimumab alone and an approximately 28 percent overall response rate for CVA21 alone," said Curti.

Among the 25 patients evaluable for safety, two had grade 3 or higher ipilimumab-related adverse events. Thus far, there have been no CVA21-related adverse events of grade 3 or higher.

"While still a small data set, we are encouraged by the low frequency of severe adverse events," said Curti. "Historically, about 25 percent of patients treated with ipilimumab have treatment-related grade 3 or higher adverse events. We have seen

this in just 8 percent of patients treated with the combination, but we will need larger numbers of patients to confirm this finding."

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