Immune checkpoint inhibitor shows early promise in previously treated lung cancer patients

January 8 2014

The PD-1 immune checkpoint inhibitor MK-3475 was well tolerated and showed durable responses in patients whose non-small cell lung cancers (NSCLC) had worsened during or after multiple prior chemotherapies, according to the results of a phase I study presented here at the AACR-IASLC Joint Conference on the Molecular Origins of Lung Cancer, held Jan. 6-9.

PD-1 is an immune checkpoint protein present on immune cells called T cells. Some cancer cells carry a protein called PD-L1 on their surfaces, and when PD-L1 attaches to PD-1 on T cells, "brakes" are applied on these T cells, thus preventing them from attacking the cancer cells. Drugs targeting PD-1, such as the antibody therapy MK-3475, can potentially release the brakes and enable T cells to perform antitumor activities.

"Previously treated lung cancers are generally managed with chemotherapy, but unfortunately, the response rates and overall survival are quite low; therefore, there is a significant unmet need for new treatment options," said Edward B. Garon, M.D., assistant professor of medicine at the David Geffen School of Medicine at the University of California, Los Angeles. "A significant percentage of patients with growing disease after two prior treatments had substantially reduced tumor volume in response to MK-3475, and the potential of this antibody drug to induce long-lasting responses in these patients is

certainly exciting and promising."

To assess the safety and antitumor activity of MK-3475 in this phase I study, Garon and colleagues recruited 38 NSCLC patients who had received at least two prior therapies, had at least one measurable tumor, were active or able to perform light work, had adequate organ function, and had an available tumor biopsy sample taken within 60 days of the first dose of MK-3475.

All patients received MK-3475 every three weeks, and their tumors were assessed by imaging techniques every nine weeks until disease progression, which was confirmed using two criteria: the immune-related response criteria (irRC) and the RECIST criteria.

At nine weeks, the objective response rates were 24 percent and 21 percent by irRC and RECIST criteria, respectively.

The investigators successfully measured PD-L1 protein expression in 33 of the 38 patients' tumor biopsies obtained prior to treatment, and determined the protein level to be greater than a cutoff point in nine patients and lower than the cutoff point in 24 patients.

Patients from the high PD-L1 group had a response rate of 67 percent and 57 percent by irRC and RECIST criteria, respectively, while patients from the low PD-L1 group had response rates of 4 percent and 9 percent by the two criteria, respectively, leading the researchers to suggest that pretreatment PD-L1 expression level may be a good predictor of response to MK-3475 treatment.

The median duration without worsening of disease among the nine responders was at least 62 weeks, and seven of the nine patients who responded to treatment were continuing to receive MK-3475 therapy at the last report, according to Garon.

About half of the patients had drug-related toxicities, the most common being rash, and there were no treatment-related deaths.

"NSCLC patients should consider clinical trials as an option for their care. Hopefully, our data will be confirmed in larger studies, and as a result, provide more treatment options for patients with this difficult-to-treat disease," said Garon.

Provided by American Association for Cancer Research