ASCO: MEDI4736 combined with tremelimumab results in acceptable toxicity in NSCLC patients

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Advanced non-small cell lung cancer (NSCLC) patients have few effective treatment options and low 5-year survival rates. The checkpoint inhibitors MEDI4736 and tremelimumab have both demonstrated acceptable safety and potential efficacy when used as single-agents in several different types of cancer. Scott J. Antonia, M.D., Ph.D., chair of the Thoracic Oncology Department at Moffitt Cancer Center will be presenting data from a phase 1b dose-escalation and expansion study of MEDI4736 combined with tremelimumab at the 2015 American Society of Clinical Oncology Annual Meeting in Chicago.

MEDI4736 is a monoclonal antibody that targets the programmed cell death-1 ligand (PD-L1) expressed on tumor cells, and tremelimumab is a monoclonal antibody that inhibits cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) found on T cells. Activation of both PD-L1 and CTLA-4 pathways blocks the immune system and inhibits the generation of an immune response. Tumor cells take advantage of this physiological process to avoid immune detection and cell death. Inhibiting these proteins with MEDI4736 and tremelimumab restimulates the immune system to detect and destroy tumor cells.

The Moffitt team and their collaborators report that MEDI4736 combined with tremelimumab resulted in manageable toxicity, with 64 percent of patients experiencing adverse events. Patients who were administered higher doses of tremelimumab with a constant dose of MEDI4736 experienced more frequent and severe toxicities. The most common overall drug-related adverse events were fatigue (26 percent), diarrhea (21 percent), and increased amylase (13 percent). Thirty-one percent of patients had one or more grade 3/4 drug-related adverse event, with the most frequent being diarrhea (8 percent) and colitis (7 percent).

Results demonstrate that the combination of MEDI4736 and tremelimumab has clinical activity in NSCLC patients, including in patients who lack tumor expression of PD-L1. Out of 31 evaluable patients, 8 patients achieved a partial response and 11 patients had stable disease, while 3 out of 10 patients with PD-L1 negative tumors had a partial response.

The maximum-tolerated dose has yet to be defined and recruitment to the study is ongoing. Trial results to date will be presented during a poster discussion session on Saturday, May 30, 3-4:15 p.m. in room S406 and during the poster session from 8-11:30 a.m. in S Hall A.

Provided by H. Lee Moffitt Cancer Center & Research Institute