Phase II trial shows activity of durvalumab in recurrent/metastatic head and neck cancer

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Analysis of the phase II CONDOR trial indicates that the immune checkpoint inhibitor durvalumab is tolerable among heavily pre-treated patients with recurrent or metastatic head and neck cancer and has the potential to slow growth in tumors with low or negative expression of the PD-L1 protein. The previously reported phase II HAWK trial demonstrated the safety and efficacy of durvalumab monotherapy in head and neck tumors that express high levels of PD-L1, and CONDOR (NCT02319044) is the first trial to show similar findings for durvalumab monotherapy in patients with low or negative PD-L1. The study will be presented today in an online news briefing and at the 2018 Multidisciplinary Head and Neck Cancers Symposium in Scottsdale, Arizona.

Cancerous cells produce proteins to stop the body's natural immune response to recognize and respond to the disease. Immune checkpoint inhibitors such as durvalumab are designed to block these so-called "checkpoint" proteins—thus allowing the immune system to remain active and attack tumors more successfully. Potential limitations with this type of immunotherapy, however, include the possibility that patients will not respond to treatment and/or that they may experience treatment-related side effects if the immune system also mistakenly targets healthy cells.

"Two immunotherapies have already been approved for use in platinum-refractory recurrent or metastatic head and neck cancer, but not all patients respond to these therapies. For immunotherapy to increase its clinical utility, it's important that we can better identify the patients who will most likely respond to treatment," said Lillian Siu, MD, lead author of the study, as well as a senior medical oncologist at Princess Margaret Cancer Centre and a professor of medicine at the University of Toronto.

"In the phase II CONDOR trial, durvalumab, an investigational PD-L1 inhibitor, showed an overall response rate consistent with other single-agent PD-1/PD-L1 inhibitors in second-line settings for head and neck cancer. Our results add to the body of evidence that this immune checkpoint inhibitor is tolerable and has demonstrated encouraging clinical activity across a range of tumors, including in heavily pre-treated recurrent or metastatic head and neck cancer."

Findings are based on 267 patients with metastatic (64% of patients) or recurrent (36%) cancer of the oral cavity, oropharynx, hypopharynx or larynx who had not responded to prior platinum-based chemotherapy, and who had low or negative expression of the PD-L1 protein. Patients were stratified by HPV and smoking status and randomized to one of three treatment arms: durvalumab alone (10 mg/kg, IV Q2W) (67 patients); tremelimumab alone (10 mg/kg IV Q4W ×7 then Q12W ×2) (67 patients); or durvalumab plus tremelimumab ([20 mg/kg D Q4W + 1 mg/kg T Q4W] ×4 then 10 mg/kg D Q2W) (133 patients). Median follow-up was 5.8 months. Responses were measured using Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1.

Safety profiles of durvalumab alone and in combination with tremelimumab were consistent with those for similar immunotherapeutic agents. Treatment-related adverse events of any grade were highest for durvalumab alone (63.1% of patients), followed by durvalumab+tremelimumab (57.9%) and tremelimumab alone (55.4%); rates for grade 3 or 4 events, conversely, were highest for tremelimumab (16.9%), followed by durvalumab+tremelimumab (15.8%) and durvalumab (12.3%). Twelve of the 267 patients

discontinued therapy due to a treatment-related adverse event, including seven patients in the combination arm and five in the tremelimumab monotherapy arm. One death in the combination therapy group was associated with treatment.

Durvalumab showed encouraging anti-tumor activity both alone and in combination with tremelimumab. Seventeen patients experienced partial responses to treatment, for overall response rates (ORR) of 9.2 percent for durvalumab alone, 7.8 percent for durvalumab+tremelimumab and 1.6 percent for tremelimumab alone. Ten of the 17 partial responses were ongoing as of March 31, 2017. The ORR rate for durvalumab monotherapy was consistent with other single-agent PD-1/PD-L1 inhibitors in this setting.

Median overall survival was 7.6 months for durvalumab+tremelimumab, 6.0 months for durvalumab and 5.5 months for tremelimumab. There was no observed difference in clinical activity between durvalumab alone and durvalumab in combination with tremelimumab.

More information: The abstract, "A Randomized, Open-Label, Multicenter, Global Phase 2 Study of Durvalumab (D), Tremelimumab (T), or D Plus T in Patients with PD-L1 Low/Negative Recurrent or Metastatic (R/M) Head and Neck Squamous Cell Carcinoma (HNSCC): CONDOR," will be presented in detail during the Plenary Session at the 2018 Multidisciplinary Head and Neck Cancers Symposium in Scottsdale, Arizona.

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