First-in-class antibody-drug conjugate shows clinical benefit against metastatic triple-negative breast cancer

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IMMU-132, an anti-Trop-2 antibody-drug conjugate (ADC) was safe, tolerable, and yielded meaningful clinical activity in heavily pretreated patients with metastatic triple-negative breast cancer (TNBC), according to data from a phase II clinical trial presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held Nov. 5–9.

"TNBC comprises about 15 to 20 percent of all invasive breast cancers diagnosed in the United States and is more prevalent in young and African-American women. It has a high recurrence rate and is perhaps the most difficult type of breast cancer to treat successfully with current cytotoxic agents. Currently, there are no targeted treatments available for TNBC," said Aditya Bardia, MD, MPH, assistant professor of medicine at Harvard Medical School, and attending physician of medical oncology at the Massachusetts General Hospital Cancer Center in Boston.

"Trop-2 is a protein present in limited amounts in normal human tissues but widely found in many human cancers. It is expressed in more than 80 percent of TNBC, making it an attractive therapeutic target," Bardia added. Sacituzumab govitecan (IMMU-132) is a first-in-class ADC, which was developed by linking approximately eight molecules of SN-38 (an active metabolite of the chemotherapy agent irinotecan) to an antibody that binds to Trop-2, he explained.

"Patients treated with other agents used to treat heavily pretreated metastatic TNBC have a median progression-free survival [PFS] of three to four months in general, while in our phase II clinical trial, patients on IMMU-132 had an interim median PFS of seven months. The response rate to standard agents is usually 10 to 20 percent, while the response rate with IMMU-132 was approximately 30 percent. If you include patients with stable disease, the clinical disease control rate, which is complete response [CR] + partial response [PR] + stable disease, was about 75 percent. Two patients had a CR to treatment, something which is rarely seen in patients with heavily pretreated metastatic TNBC," Bardia said.

"We hope that this drug can be further developed and, if approved, provide a significantly better alternative for these patients with poor prognosis," Bardia said. IMMU-132 received Fast Track designation from the U.S. Food and Drug Administration for the treatment of patients with TNBC, he added.

As of October 2015, Bardia and colleagues had enrolled in the multicenter phase II trial 83 TNBC patients who had not responded to previous treatments or had relapsed after successful treatment. The first patient was enrolled into this study 31 months ago. All patients received IMMU-132 once a week for 2 weeks followed by one week of rest. This treatment cycle was repeated until the patient had disease progression or withdrew from the trial. Patients were evaluated for safety every week and assessed for response every two months.

For the 54 patients with 2 or more prior lines of treatment that included a taxane who had received IMMU-132 at the 10 mg/kg dose level, the overall response rate, defined as CR plus PR, was 31.5 percent, and included two CRs.

"One of the most interesting findings is that the agent was well tolerated

by patients, and toxicity was much lower than one would anticipate with chemotherapy agents such as irinotecan," Bardia said. Grade 3 to 4 toxicities included neutropenia (in 15 percent of the patients), anemia (6 percent), diarrhea (6 percent), and febrile neutropenia (4 percent), and no patient discontinued treatment because of toxicity issues.

Twenty-two patients continue to receive treatment, and the overall survival data are not yet mature, with 87 percent of patients still alive, Bardia noted.

Limitations of the study include lack of a placebo arm and small sample size, according to Bardia.

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