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New, investigational PARP1/2 inhibitor BGB-290 shows promise

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Treatment with BGB-290, a new, investigational, highly selective inhibitor of PARP1/2, was safe, tolerable, and yielded clinical responses in patients with advanced ovarian cancer, according to data from a phase I clinical trial presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held Nov. 5–9.

As of June 30, 2015, 29 patients with relapsed or refractory solid tumors had been enrolled in the clinical trial. Among the 14 ovarian cancer patients for whom there were evaluable data, seven had an objective response, as assessed by RECIST 1.1 criteria. One was a complete response and six were partial responses. One of the six patients with a partial response had disease progression and withdrew from the trial after being treated with BGB-290 for 420 days. All other responders remained on treatment with response sustained.

"Targeting PARP proteins has been established to be effective for the treatment of ovarian cancer in women who have germline BRCA mutations," said Jason Yang, MD, PhD, senior vice president and head of clinical development at BeiGene in Beijing, China. "BGB-290 is a highly specific PARP1/2 inhibitor, which could potentially translate into better safety and tolerability compared with other PARP inhibitors.

"In this first-in-human phase I clinical trial, BGB-290 was found to be well tolerated," continued Yang. "The trial also established proof-of-concept, with antitumor activity seen starting at the lowest tested dose

and data suggestive of a wide therapeutic window. Based on the preliminary safety and efficacy data, we are considering phase II clinical trials in several different cancer types, including ovarian cancer."

As of June 30, 2015, the 29 patients enrolled so far in the clinical trial had a range of types of solid tumors. Nineteen had ovarian cancer and 10 had other types of cancer, including small-cell lung cancer, glioblastoma, breast cancer, non–small cell lung cancer, gastric cancer, and leiomyosarcoma. They received escalating doses of BGB-290—2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg, 60 mg, and 80 mg—orally twice a day (BID). BGB-290 was well tolerated at all doses. The maximum-tolerated dose has not been reached; dose escalation is continuing.

The most common adverse events have been grades 1 and 2 fatigue and nausea. There were four grade 3 adverse events in patients receiving 20 mg (1) and 40 mg (3) BGB-290 BID.

Of the 14 evaluable patients with ovarian cancer, the seven patients who had an objective response were treated at a range of dose levels from 2.5 mg to 60 mg BGB-290 BID. Five of these ovarian cancer patients had germline BRCA mutations. Patients treated at 80 mg BID were not yet evaluable as of June 30, 2015.

Yang explained that the major limitation of the current study is that this is an early-phase study with only a small number of patients treated so far.

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